JOC The Journal of Organic Chemistry

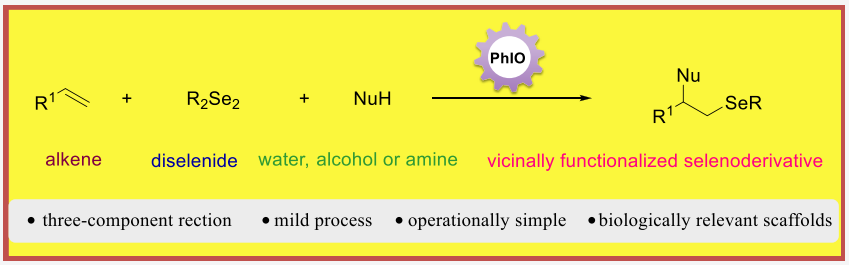
pubs.acs.org/joc Article

Iodosobenzene-Mediated Three-Component Selenofunctionalization of Olefins

Zhi-Peng Liang, Wei Yi,† Peng-Fei Wang,† Gong-Qing Liu,* and Yong Ling*

Cite This: J. Org. Chem. 2021, 86, 5292−5304 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

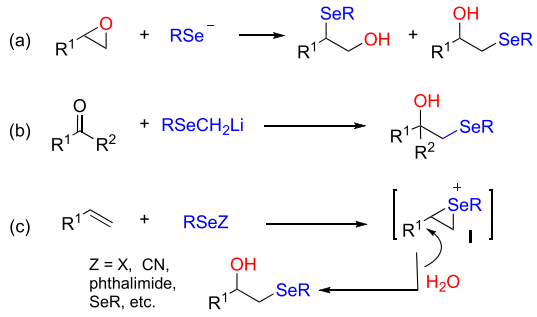


ABSTRACT: A three-component reaction of olefin, diselenide and water, alcohols, phenol, carboxylic acid, or amine by a commercially available hypervalent iodine(III) reagent, PhIO, was developed. This method provides access to a wide range of vicinally functionalized selenoderivatives under ambient conditions with mostly excellent yields and high diastereoselectivity. The developed reaction displays high levels of functional group compatibility and is suitable for the late-stage functionalization of styrene-functionalized biomolecules. Preliminary investigations on the mechanism of the reaction are also presented.

INTRODUCTION

The introduction of selenium into organic molecules has recently been the subject of intense research, as selenium-containing molecules have found widespread applications in the fields of organic synthesis and drug discovery.[1] Within the wide variety of organoselenium compounds, β-hydroxy selenides represent particularly versatile manifolds, as documented in access to some of the extremely biologically important natural products, such as pancratistatin,[2] sphingosine,[3] and schweinfurthin B.[4] Additionally, these compounds can be readily converted to allylic alcohols,[5] olefins,[6] vinyl selenides,[7] and heterocyclic compounds[8] through classical reactions. Consequently, numerous attempts have been made to determine the synthetic route to access β-hydroxy selenides. Traditional approaches to synthesize this class of compounds involve the ring-opening reactions of epoxides with selenolate anions, such as (phenylseleno)silanes,[9] aluminum selenolates,[10] zinc selenolates,[11] selenoboranes,[12] benzeneselenol[13] selenostannanes,[14] and selenium powder[15] (Scheme 1a). Most selenolate anions are relatively unstable and are usually formed in situ by reductive cleavage of the Se−Se bond or by the insertion of selenium into organometallic reagents under controlled anhydrous conditions. Furthermore, these approaches are commonly implemented under acidic conditions and, thus, suffer from poor tolerance to base-sensitive functional groups as well as low regioselectivity. Another common synthetic strategy toward β-hydroxy selenides involves the nucleophilic addition of α-selenoalkyllithiums or analogues to carbonyl compounds (Scheme 1b).[5a,16] The

Scheme 1. β-Hydroxy Selenides: State-of-the-Art



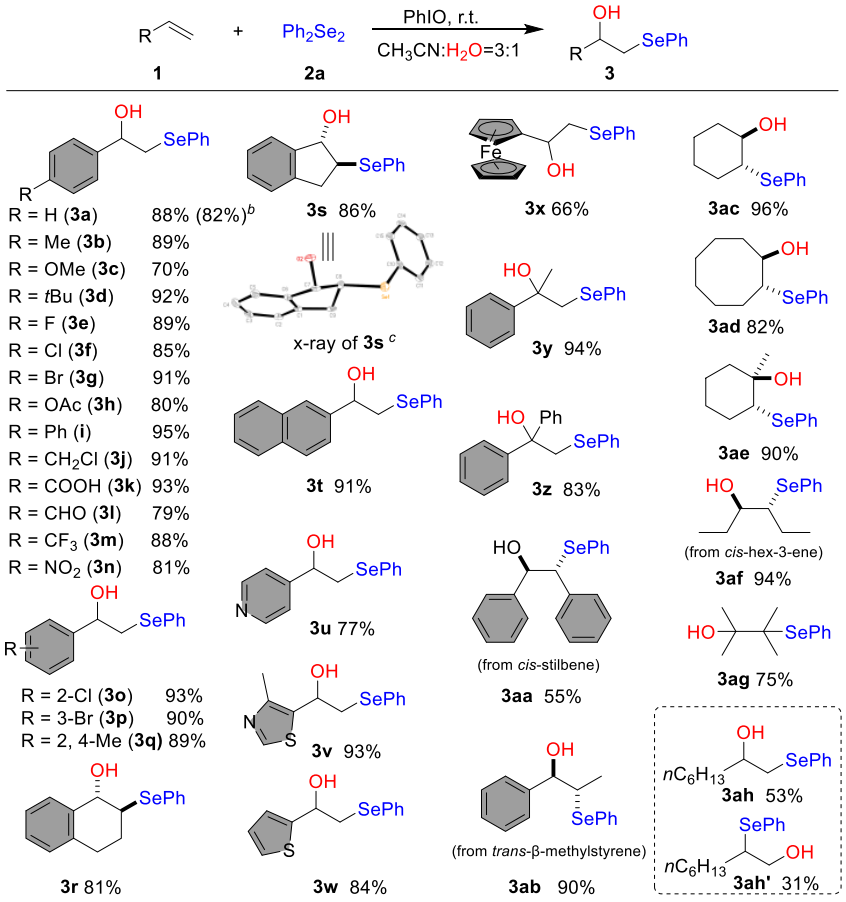
preparations and reactions of α-selenoalkyllithiums, however, often require very low temperature (usually at −78 °C) and anhydrous conditions, which causes inconvenient handling procedures.

In recent years, the selenofunctionalization of simple alkenes has developed into a powerful tool for the preparation of selenocompounds because this process enables the simultaneous introduction of selenium functional groups and other synthetically useful functionalities across the π system in an

Received: February 2, 2021
Published: March 11, 2021

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

Scheme 2. Scope of Alkenes[a]



[a]Reactions were performed in the presence of alkene **1** (0.25 mmol), Ph_2Se_2 **2a** (0.25 mmol), PhIO (0.25 mmol), and CH_3CN/H_2O (3:1, 2.0 mL) in an open flask at room temperature for 20 h. [b]Five mmol scale. [c]ORTEP drawing of **3s** with the thermal ellipsoids at 30% probability. Hydrogen atoms were omitted for clarity.

atom-economical fashion with increasing molecular complexity.[17] In this context, oxyselenation of alkenes has been proven to be a step- and atom-economical route for the preparation of *β*-hydroxy selenides (Scheme 1c). Mechanistically, this process occurs via the formation of seleniranium intermediate **I** and subsequent nucleophilic attack of water at the more electrophilic carbon. In recent decades, great attention has been devoted to seeking suitable selenium sources, which can serve as reactive electrophilic intermediates to induce the generation of seleniranium ion **I**. From a conceptual point of view, two different strategies have been chosen: directly using electrophilic selenenylating agents, such as phenylselenenyl halides,[18] phenyl selenocyanate,[19] or *N*-phenylselenophthalimide,[20] or preparing electrophilic selenium species in situ by the oxidation of diselenides through electrochemical processes[21] or by the use of oxidants, such as Oxone,[22] 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ),[23] hypervalent iodine reagent,[24] ammonium persulfate,[25] or *m*-chloroperbenzoic acid.[26] Although they represent useful platforms for *β*-hydroxy selenides, the preparation and handling of toxic and moisture-sensitive selenylating agents,[18] the necessity to perform the reactions in the presence of transition metals[18a,19] and nonoptimal chemical yields[26] narrow the practical applicability of these methods.

Tingoli et al. demonstrated the synthesis of phenylseleno-acetoxylation, hydroxylation, etherification, and lactonization products by the treatment of diphenyl diselenide (Ph_2Se_2) with iodobenzene diacetate in acetonitrile.[24a] The limitation of this procedure was that acetoxyphenylselenenylation products were obtained for intermolecular variant reactions because of the presence of the nucleophilic acetate anion as an iodine(III) ligand, and only isolated examples have been demonstrated on the preparation of *β*-hydroxy selenides; the scope of diselenides was confined to Ph_2Se_2. Moreover, a detailed understanding of mechanistic aspects still needs to be illuminated.

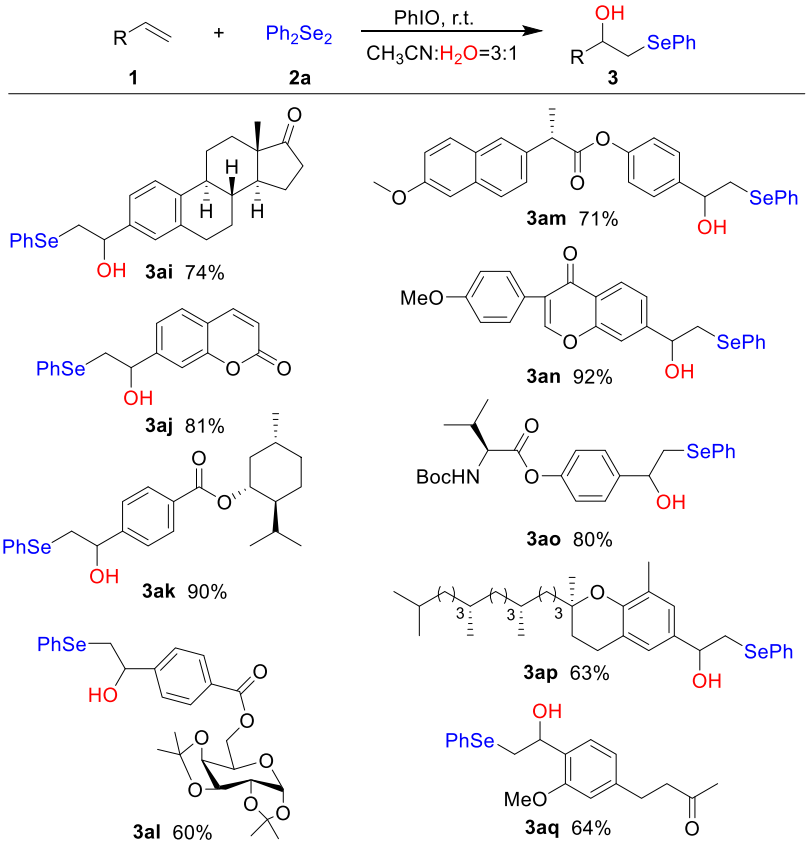
From the careful analysis of these drawbacks and limitations and in continuation of our ongoing work toward the hypervalent iodine-promoted difunctionalization of olefins,[27] we conjecture that the in situ generated active electrophilic selenium species from iodosobenzene (PhIO) and diselenide would form seleniranium ion **I** with alkene and subsequent intermolecular attack by an array of nucleophiles including water, alcohol, acid or amine, generating vicinal difunctional compounds that may overcome the aforementioned limitations and provide an efficient and modular approach for the formation of diverse selenium-containing compounds.

RESULTS AND DISCUSSION

With this in mind, we investigated the oxyselenation of styrene (**1a**) with Ph_2Se_2 (**2a**) in the presence of PhIO in a mixture of water and acetonitrile. To our delight, the title reaction

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

Scheme 3. Scope of Vinylarenes Derived from Biomolecules[a]



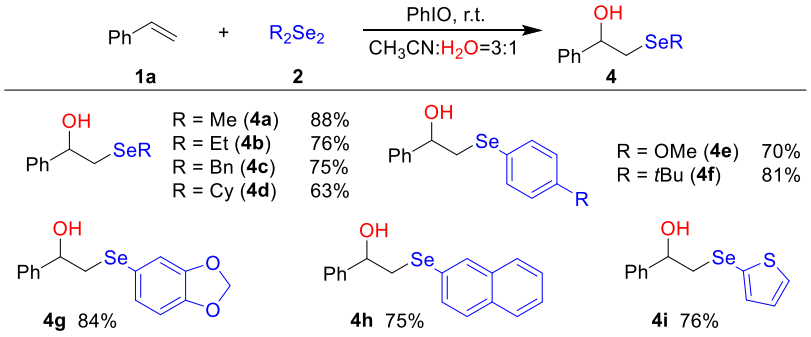
[a]Reactions were performed in the presence of alkene **1** (0.25 mmol), Ph_2Se_2 **2a** (0.25 mmol), PhIO (0.25 mmol), and CH_3CN/H_2O (3:1, 2.0 mL) in an open flask at room temperature for 20 h.

proceeded readily and provided a Markovnikov product exclusively, *β*-hydroxy selenide **3a**, with an 88% yield and complete regioselectivity.[28] Notably, the present reaction can be scaled up to a 5 mmol scale without significant decreases in the yield, suggesting that this simple protocol could be employed as a practical method to access *β*-hydroxy selenides. Encouraged by these results, other alkenes were then subjected to the same conditions to test the scope of the reaction, and the results are summarized in Scheme 2.

As shown in Scheme 2, an array of substituted vinylarenes readily underwent oxyselenation to produce the corresponding *β*-hydroxy selenides **3a**−**3q** with yields up to 95%. The electronic effect of the arenes had little impact on the course of the reaction, and terminal vinylarenes bearing either electron-donating or electron-withdrawing substituents all delivered the corresponding products in good to excellent yields. Notably, a large variety of functional groups at the styrene aromatic core could be tolerated, including halide, ester, carboxyl, formyl, trifluoromethyl, and nitro groups. The resulting products from this transformation provide a facile approach toward the synthesis of versatile motifs of many biologically active selenium-containing compounds. For example, the use of Cl- and Br-substituted styrenes allows for the further modification of products **3f**−**3g** and **3o**−**3p** by means of classical Pd-catalyzed cross-couplings. In addition, ester, carboxyl, formyl, and nitro groups can be manipulated readily to give various functionalized selenoderivatives using conventional reactions. Next, more rigid alkenes, such as 1,2-dihydronaphthalene **1r** and indene **1s**, were examined under the optimized conditions and gave the desired products **3r**−**3s** exclusively with *trans*-diastereoselectivity and good yields. The relative configuration of **3s** was elucidated based on X-ray crystallography.[29] Furthermore, naphthalene-derived substrates and heteroaromatic olefins, such as 4-vinylpyridine, 5-vinylthiazole 2-vinylthiophene, and vinylferrocene, were subjected to the same reaction to test the scope of the reaction and gave the corresponding products at acceptable yields (**3t**−**3x**). Subsequently, the possibility of performing these reactions with 1,1-disubstituted (**1y**−**1z**) and internal alkenes (**1aa**−**1ab**) was investigated. The *cis*-stilbene **1aa**, however, resulted in a drastic reduction in the reaction yield, probably due to the steric hindrance of this substrate. Finally, aliphatic alkenes were also suitable substrates for the current transformation and produced desired products **3ac**−**3ah′** in good yields, but resulted in a mixture of regioisomers corresponding to Markovnikov-type hydroxyselenated product (**3ah**) and an anti-Markovnikov-type adduct (**3ah′**) in a relative ratio of 1.7:1 in the case of 1-octene. The total yield and the isomer ratio of **3ah** and **3ah′** were hardly affected by the reverse addition of the reactants. Comparison of regioselectivity in the case of aryl alkenes **1a**−**1ab** with alkyl alkene **1ah** clearly demonstrates predominant intermediate stabilization over steric interaction for cases of **1a**−**1ab**; however, **1ah** gave a mixture of Markovnikov and anti-Markovnikov adducts, which could be ascribed to the variation in the charge density on the two carbons leading to a nonregiospecific ring-opening of the seleniranium ion intermediate with water. Thus, the seleniranium intermediate was attacked by H_2O at the less sterically hindered C atom yielding

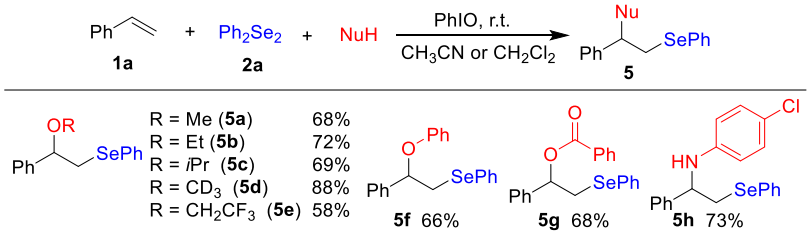
https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

Scheme 4. Scope of Diselenides[a]



[a]Reactions were performed in the presence of styrene **1a** (0.25 mmol), R_2Se_2 **2** (0.25 mmol), PhIO (0.25 mmol), and CH_3CN/H_2O (3:1, 2.0 mL) in an open flask at room temperature for 20 h.

Scheme 5. Scope of Other Nucleophiles[a]



[a]For **5a**−**5e**, reactions were performed in the presence of styrene **1a** (0.25 mmol), Ph_2Se_2 **2a** (0.25 mmol), PhIO (0.25 mmol), and CH_3CN/ROH (3:1, 2.0 mL) in an open flask at room temperature for 20 h. For **5f**−**5h**, reactions were performed in the presence of styrene **1a** (0.25 mmol), Ph_2Se_2 **2a** (0.25 mmol), PhIO (0.25 mmol), nucleophile (1.0 mmol), and CH_2Cl_2 (2.0 mL) in an open flask at room temperature for 20 h.

an anti-Markovnikov adduct. Remarkably, all reactions described here displayed excellent diastereoselectivity, producing one single diastereomer (**3aa**−**3af**). The stereochemical course of title reaction was disclosed to be *trans* from the oxyselenation of *trans*- and *cis*-alkene, which afforded the *erythro*- and *threo*-type hydroxyselenated product, respectively. For example, hydroxyselenation of *trans*-*β*-methylstyrene afforded *erythro*-**3ab**, while *cis*-alkene, such as **1aa** and **1af**, yielded *threo*-**3aa** and **3af**. The high diastereoselectivity may be attributed to the stereospecific ring-opening of the putative seleniranium ion intermediate **I**.[18c,30]

To further evaluate the synthetic utility and generality of the current procedure, more complex styrene-functionalized biomolecules were investigated. As shown in Scheme 3, the late-stage oxyselenation of biologically active molecules was successful, giving the corresponding *β*-hydroxy selenides. For instance, natural product derivatives, such as coumarin (**1aj**), L-menthol (**1ak**), galactose (**1al**), formononetin (**1an**), and vanillylacetone (**1aq**), and pharmaceutical intermediates, such as estrone (**1ai**), naproxen (**1am**), and tocopherol (**1ap**), and peptide (**1ao**) derivatives, were tolerated and produced desired products **3ai**−**3aq** with good yields.

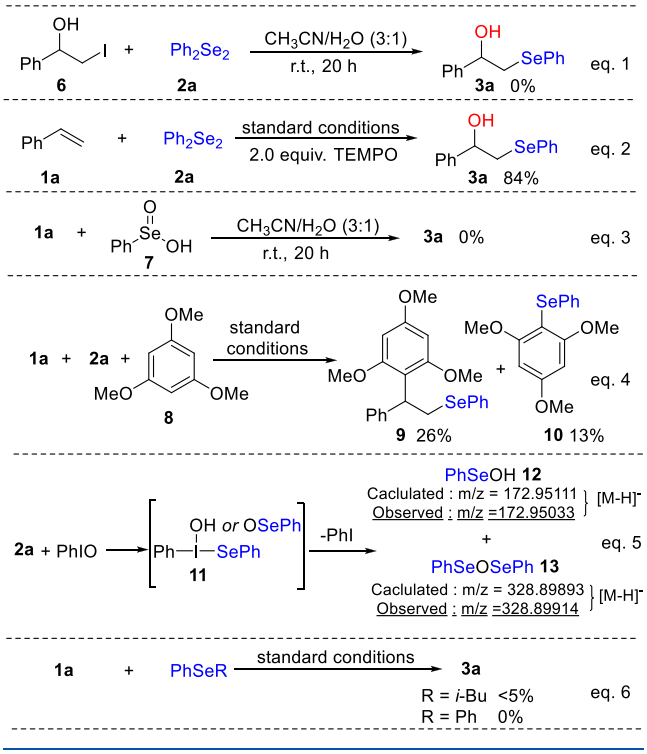
Inspired by these results, we next explored the versatility of the title reaction by probing diverse diselenides. As depicted in Scheme 4, aliphatic diselenides were efficiently engaged in this process, with styrene **1a** delivering desired products (**4a**−**4d**) with good yields. The other substituted diphenyl diselenides and heteroaryl diselenide were also good reaction partners and produced the corresponding selenides (**4e**−**4i**) in moderate to good yields.

Encouraged by the successful application of a water nucleophile, we then switched the solvent system to alcohol, which would enable the synthesis of *β*-alkoxy selenides in a straightforward transformation. As expected, the title reaction system proceeded readily in a mixture of different alcohols and acetonitrile and gave *β*-alkoxy selenides in good yields exclusively with Markovnikov selectivity (Scheme 5). Notably, this protocol is also effective for the synthesis of deuterated functionalized selenide compound **5d** through the utilization of deuterated methanol as a nucleophilic solvent. Next, other tested nucleophiles, such as phenol, carboxylic acid, and amine, were further examined. Gratifyingly, slight modifications to the optimal reaction conditions allowed the preparation of a variety of vicinally functionalized selenoderivatives (**5f**−**5h**) with good yields.

With regard to the mechanism of the title transformation, the following observations from control experiments are noteworthy. First, when iodohydrin **6** was stirred for 20 h in a mixture of water and acetonitrile, it remained intact and was totally recovered, and no trace of **3a** was detected (Scheme 6, eq 1). These results indicate that a cascade process of iodohydroxylation of styrene and subsequent nucleophilic substitution of the C−I bond by arylselenide is less likely. Second, no significant effect on the reaction outcomes was observed after the addition of the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), which indicates that a radical process seems very unlikely (Scheme 6, eq 2). Ph_2Se_2 has been documented to be readily oxidized to phenylseleninic acid ($PhSeO_2H$) **7** in the presence of an oxidant,[31] and thus, whether **7** the active electrophilic species in the present reaction was investigated. None of the *β*-hydroxy selenide **3a** was, however, detected when commercially available $PhSeO_2H$ **7** was used (Scheme 6, eq 3). These studies suggest that acid **7** might not be the intermediate of the developed transformation. Interestingly, when 1,3,5-trimethoxybenzene **8** was employed as a nucleophile under the title reaction condition, a yield of

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

Scheme 6. Experiments for Mechanistic Studies

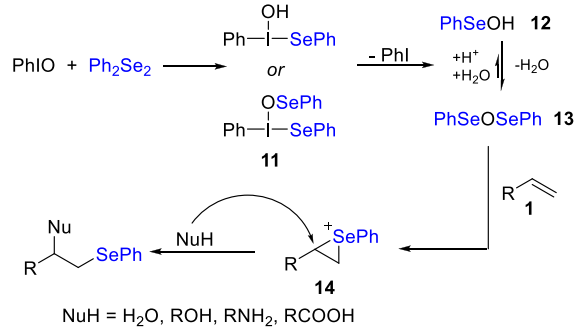


26% of the desired carboselenenylation product **9** was obtained along with some amounts of selenation product **10** (Scheme 6, eq 4). Compound **10** probably arose from an electrophilic attack of the phenylselenenyl cation ($PhSe^+$) on the electron-rich 1,3,5-trimethoxybenzene.[32] These results suggest that the current transformation should be an electrophilic process. However, it is still necessary to identify the authentic active electrophilic species in this transformation.

To examine true reactive organoselenium species in the reaction, NMR experiments were carried out, and the results showed no interaction of styrene with Ph_2Se_2 (Figure S1). PhIO is insoluble in $CDCl_3$ because it displays a zigzag polymeric chain structure according to X-ray powder diffraction and EXAFS studies,[33] and the ^1H NMR spectrum of PhIO and its mixture with styrene thus cannot be recorded. PhIO, however, could be mostly dissolved when Ph_2Se_2 was added to the $CDCl_3$ solution. This result indicates that PhIO can react with Ph_2Se_2 to generate new reactive species during the course of the reaction. This phenomenon was in accordance with NMR observations, which showed that the signal pattern for the aromatic protons of Ph_2Se_2 changed significantly after the addition of PhIO, indicating the mutual interaction between Ph_2Se_2 and PhIO and, thus, resulting in changes in the electronic environment surrounding the phenyl groups in Ph_2Se_2 (Figure S2). Based on our understanding of hypervalent iodine chemistry, we assumed that PhIO can react with Ph_2Se_2 to generate benzeneselenenic acid (PhSeOH) **12** and/or its anhydride **13** as the active species through the reaction of Ph_2Se_2 with PhIO to give putative intermediate **11**,[34] followed by the elimination of iodobenzene (Scheme 6, eq 5). The formation of iodobenzene was confirmed by ^{13}C NMR experiments and GC−MS analysis (Figures S3 and S4). PhSeOH **12** cannot be isolated in analytically pure at this stage, as it is a notoriously unstable compound,[35] but it can be detected by HRMS experiments. A mass peak at *m/z* 172.95033 was detected from the reaction of Ph_2Se_2 and PhIO, implying the generation of PhSeOH **12** during the reaction (Figure S5). Additionally, its anhydride **13** was also detected on ESI-MS (Figure S6). To further certify whether PhSeOH **12** could be the active electrophilic species in the reaction, alkyl phenyl selenides were subjected to the reaction because PhSeOH is the side product of the well-known selenoxide *syn*-elimination of these selenides.[36] As shown in Scheme 6, eq 6, *i*-BuSePh gave a trace amount of the desired **3a** probably due to difficulties in the oxidation of *i*-BuSePh to the corresponding selenoxide under the title conditions. As expected, PhSePh failed to produce any *β*-hydroxy selenide **3a** because PhSePh is incapable of undergoing selenoxide *syn*-elimination to generate PhSeOH. Thus, these results implied that putative intermediate PhSeOH **12**, generated in situ from PhIO and Ph_2Se_2, should be involved in this reaction.

On the basis of the above results and previous literature reports,[24a,37] a preliminary reaction pathway is proposed in Scheme 7. First, Ph_2Se_2 is oxidized by PhIO to generate

Scheme 7. Tentative Reaction Pathway



intermediate PhSeOH **12** and/or it anhydride **13**. We believe **13** rather than **12** would serve as a reactive electrophilic intermediate to react with alkene **1** to give seleniranium intermediate **14** because extremely unstable PhSeOH **12** has been documented to readily convert to anhydride **13** through the self-condensation process.[35] Finally, trapping of **14** with various nucleophiles delivers the vicinally functionalized selenoderivatives.

CONCLUSION

In conclusion, we have developed a PhIO-promoted three-component coupling of olefin, diselenide and water, alcohols, phenol, carboxylic acid, or amine for the synthesis of vicinally functionalized selenoderivatives. The title transformation allows for significant variation within each of the three components and displays high diastereoselectivity. Mechanistically, the process is believed to proceed through the transient formation of an electrophilic selenium intermediate derived from the oxidation of diselenide by PhIO. Owing to its mild reaction conditions, easy operation, excellent functional group tolerance, and suitability for the late-stage functionalization of complex molecules of biological importance, we envisage that the present protocol will have a widespread application in the construction of diverse selenium-containing compounds.

EXPERIMENTAL SECTION

General Experimental Information. Reagents were used as received without further purification unless otherwise indicated. Solvents were dried and distilled prior to use. Petroleum ether used

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

had a boiling point range of 60−90 °C. Diselenides were prepared from the corresponding iodides with elemental selenium, according to Braga's report.[38] Chromatographic purification of products was performed as flash column chromatography on silica gel (200−300 meshes). Thin-layer chromatography (TLC) was carried out on silica plates (TLC Silica GF_{254}). Visualization of the compounds was accomplished by projecting UV light onto the developed plates. Nuclear magnetic resonance spectra were recorded at an ambient temperature (unless otherwise stated) at 400 MHz (100 MHz for ^{13}C) in $CDCl_3$. Chemical shifts were reported in ppm (δ) using TMS as an internal standard, and spin−spin coupling constants (J) were given in hertz. Multiplicities of NMR signals are abbreviated as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectrometry (HRMS) analyses were carried out on a Thermo Fisher Q_Exactive Mass Spectrometer, and the mass analyzer type is Orbitrap. The crystal of compound **3s** was obtained by slowly evaporating a mixture of ethyl acetate and *n*-hexane solution (1:5) at an ambient temperature. The data were collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero, equipped with an AtlasS2 CCD using Cu Kα radiation. Melting points were determined on glass slides using a digital display microscopic melting point apparatus and were presented uncorrected.

General Procedure for Selenofunctionalization of Olefins. The reaction was carried out in an open air system at an ambient temperature. To a 10 mL vessel with a magnetic stir bar were added 0.25 mmol alkene, 0.25 mmol diselenide, 0.25 mmol PhIO, and 2 mL of CH_3CN/water or CH_3CN/alcohol (3:1). The reaction mixture was stirred overnight. The reaction was monitored by TLC. After completion of the reaction (ca. 20 h), the mixture was added to 5 mL of H_2O and extracted with ethyl acetate (15 mL) three times. The combined organic layer was dried (Na_2SO_4) and concentrated to give the crude residue, which was purified by flash column chromatography to give the corresponding product.

1-Phenyl-2-(phenylselanyl)ethan-1-ol (3a). Compound **3a** was prepared according to the general procedure and isolated as an oil (61 mg, 88% yield) after flash chromatography (petroleum ether/ethyl acetate = 15:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.8−7.45 (m, 2H), 7.26−7.23 (m, 4H), 7.23−7.16 (m, 4H), 4.66 (dd, J = 9.4, 3.7 Hz, 1H), 3.22 (dd, J = 12.8, 3.7 Hz, 1H), 3.06 (dd, J = 12.8, 9.4 Hz, 1H), 2.75 (brs, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.4, 132.1, 128.2, 128.1, 127.5, 126.9, 126.4, 124.76, 71.2, 37.4. Spectral data are in agreement with literature values.[22]

2-(Phenylselanyl)-1-(p-tolyl)ethan-1-ol (3b). Compound **3b** was prepared according to the general procedure and isolated as an oil (65 mg, 89% yield) after flash chromatography (petroleum ether/ethyl acetate = 18:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46−7.44 (m, 2H), 7.23−7.17 (m, 3H), 7.16−7.10 (m, 2H), 7.05 (d, J = 7.7 Hz, 2H), 4.63 (dt, J = 8.9, 3.0 Hz, 1H), 3.19 (dd, J = 12.7, 3.9 Hz, 1H), 3.05 (dd, J = 12.7, 9.2,Hz, 1H), 2.76 (d, J = 2.6 Hz, 1H), 2.25 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 138.5, 136.6, 132.0, 128.2, 128.15, 128.13, 126.3, 124.7, 71.0, 37.3, 20.1. Spectral data are in agreement with literature values.[22]

1-(4-Methoxyphenyl)-2-(phenylselanyl)ethan-1-ol (3c). Compound **3c** was prepared according to the general procedure and isolated as an oil (54 mg, 70% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.58−7.39 (m, 2H), 7.31−7.07 (m, 5H), 6.79 (d, J = 8.7 Hz, 2H), 4.64 (dt, J = 9.3, 3.2 Hz, 1H), 3.72 (s, 3H), 3.20 (dd, J = 12.7, 3.8 Hz, 1H), 3.07 (dd, J = 12.7, 9.3 Hz, 1H), 2.68 (d, J = 2.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 158.3, 133.6, 132.0, 128.2, 128.1, 126.3, 126.0, 112.7, 70.8, 54.3, 37.4. Spectral data are in agreement with literature values.[22]

1-(4-(*tert*-Butyl)phenyl)-2-(phenylselanyl)ethan-1-ol (3d). Compound **3d** was prepared according to the general procedure and isolated as an oil (77 mg, 92% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.48−7.36 (m, 2H), 7.31−7.20 (m, 2H), 7.18−7.16 (m, 5H), 4.64 (dt, J = 9.2, 3.2 Hz, 1H), 3.19 (dd, J = 12.7, 3.9 Hz, 1H), 3.06 (dd, J = 12.8, 9.2 Hz, 1H), 2.77 (d, J = 2.7 Hz, 1H), 1.21 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.8, 138.4, 131.9, 128.3, 128.1, 126.2, 124.5, 124.4, 71.1, 37.1, 33.5, 30.3. Spectral data are in agreement with literature values.[26]

1-(4-Fluorophenyl)-2-(phenylselanyl)ethan-1-ol (3e). Compound **3e** was prepared according to the general procedure and isolated as an oil (66 mg, 89% yield) after flash chromatography (petroleum ether/ethyl acetate = 16:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.42 (m, 2H), 7.27−7.11 (m, 5H), 6.91 (t, J = 8.7 Hz, 2H), 4.62 (dt, J = 9.2, 3.2 Hz, 1H), 3.16 (dd, J = 12.8, 3.9 Hz, 1H), 3.00 (dd, J = 12.8, 9.3 Hz, 1H), 2.87 (d, J = 2.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.3 (d, C−F, $^1J_{C-F}$ = 246.0 Hz), 137.2 (d, C−F, $^3J_{C-F}$ = 3.1 Hz), 132.1, 128.2, 127.9, 126.5, 126.4 (d, C−F, $^3J_{C-F}$ = 3.1 Hz), 114.3 (d, C−F, $^2J_{C-F}$ = 21.5 Hz) 70.5, 37.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ −114.3. Spectral data are in agreement with literature values.[15a]

1-(4-Chlorophenyl)-2-(phenylselanyl)ethan-1-ol (3f). Compound **3f** was prepared according to the general procedure and isolated as an oil (66 mg, 85% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.65−7.29 (m, 2H), 7.30−7.00 (m, 7H), 4.60 (dt, J = 9.2, 3.1 Hz, 1H), 3.16 (dd, J = 12.8, 3.8 Hz, 1H), 2.98 (dd, J = 12.8, 9.3 Hz, 1H), 2.88 (d, J = 2.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 139.9, 132.5, 132.2, 128.3, 127.8, 127.6, 126.5, 126.2, 70.4, 37.3. Spectral data are in agreement with literature values.[22]

1-(4-Bromophenyl)-2-(phenylselanyl)ethan-1-ol (3g). Compound **3g** was prepared according to the general procedure and isolated as an oil (81 mg, 91% yield) after flash chromatography (petroleum ether/ethyl acetate = 16:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49−7.39 (m, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.22−7.16 (m, 3H), 7.09 (d, J = 8.4 Hz, 2H), 4.58 (dt, J = 9.1, 3.3 Hz, 1H), 3.14 (dd, J = 12.8, 3.9 Hz, 1H), 2.97 (dd, J = 12.8, 9.2 Hz, 1H), 2.91 (d, J = 2.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 140.4, 132.2, 130.5, 128.3, 127.7, 126.5, 120.6, 70.5, 37.2. Spectral data are in agreement with literature values.[15a]

4-(1-Hydroxy-2-(phenylselanyl)ethyl)phenyl acetate (3h). Compound **3h** was prepared according to the general procedure and isolated as an oil (67 mg, 80% yield) after flash chromatography (petroleum ether/ethyl acetate = 8:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.53−7.37 (m, 2H), 7.26 (d, J = 8.6 Hz, 2H), 7.21−7.19 (m, 3H), 6.97 (d, J = 8.6 Hz, 2H), 4.65 (dt, J = 9.1, 3.0 Hz 1H), 3.19 (dd, J = 12.8, 3.7 Hz, 1H), 3.02 (dd, J = 12.8, 9.5 Hz, 1H), 2.85 (brs, 1H), 2.21 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 168.5, 149.1, 139.0, 132.1, 128.3, 128.0, 126.4, 125.9, 120.6, 70.7, 37.4, 20.1. Spectral data are in agreement with literature values.[26]

1-([1,1′-Biphenyl]-4-yl)-2-(phenylselanyl)ethan-1-ol (3i). Compound **3i** was prepared according to the general procedure and isolated as a white solid (84 mg, 95% yield) after flash chromatography (petroleum ether/ethyl acetate = 17:1). Mp: 70−72 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.49−7.38 (m, 6H), 7.35−7.18 (m, 5H), 7.16−7.10 (m, 3H), 4.66 (dt, J = 9.2, 3.2 Hz, 1H), 3.19 (dd, J = 12.7, 3.9 Hz, 1H), 3.04 (dd, J = 12.7, 9.2 Hz, 1H), 2.91 (d, J = 2.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 140.4, 139.7, 139.6, 132.0, 128.2, 128.1, 127.7, 126.3, 126.2, 126.1, 126.0, 125.2, 71.0, 37.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{19}OSe$, 355.0596; found, 355.0596.

1-(4-(Chloromethyl)phenyl)-2-(phenylselanyl)ethan-1-ol (3j). Compound **3j** was prepared according to the general procedure and isolated as an oil (74 mg, 91% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.41 (m, 2H), 7.29−7.07 (m, 7H), 4.63 (dd, J = 9.4, 3.8 Hz, 1H), 4.46 (s, 2H), 3.16 (dd, J = 12.8, 3.8 Hz, 1H), 3.00 (dd, J = 12.8, 9.2 Hz, 1H), 2.90 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.7, 136.0, 132.0, 128.2, 128.0, 127.7, 126.4, 125.2, 70.8, 44.9, 37.2. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{15}H_{14}ClSe$, 308.9944; found, 308.9937.

4-(1-Hydroxy-2-(phenylselanyl)ethyl)benzoic acid (3k). Compound **3k** was prepared according to the general procedure and isolated as a yellow solid (75 mg, 93% yield) after flash chromatography (petroleum ether/ethyl acetate = 1:2). Mp: 90−92 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.1 Hz, 2H), 7.48

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

(dd, J = 6.6, 2.9 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.26−7.15 (m, 3H), 4.72 (dd, J = 9.4, 3.6 Hz, 1H), 3.24 (dd, J = 12.9, 3.6 Hz, 1H), 3.02 (dd, J = 12.9, 9.4 Hz, 1H), 1.12(s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 147.3, 132.3, 129.4, 128.3, 127.7, 127.5, 126.7, 124.9, 70.6, 37.4. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{15}H_{13}O_2Se$, 305.0075; found, 305.0072.

4-(1-Hydroxy-2-(phenylselanyl)ethyl)benzaldehyde (3l). Compound **3l** was prepared according to the general procedure and isolated as an oil (60 mg, 79% yield) after flash chromatography (petroleum ether/ethyl acetate = 1:2). ^1H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.51−7.46 (m, 2H), 7.43 (d, J = 8.2 Hz, 2H), 7.25−7.17 (m, 3H), 4.72 (dd, J = 9.4, 3.6 Hz, 1H), 3.24 (dd, J = 12.9, 3.6 Hz, 1H), 3.01 (dd, J = 12.9, 9.4 Hz, 1H), 3.00 (brs, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 190.9, 148.1, 134.9, 132.4, 129.0, 128.4, 127.5, 126.7, 125.4, 70.5, 37.4. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{15}H_{13}OSe$, 289.0126; found, 289.0125.

2-(Phenylselanyl)-1-(4-(trifluoromethyl)phenyl)ethan-1-ol (3m). Compound **3m** was prepared according to the general procedure and isolated as an oil (76 mg, 88% yield) after flash chromatography (petroleum ether/ethyl acetate = 15:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.1 Hz, 2H), 7.44−7.39 (m, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.21−7.17 (m, 3H), 4.67 (dt, J = 9.2, 3.1 Hz, 1H), 3.18 (dd, J = 12.9, 3.8 Hz, 1H), 3.05−2.91 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.3, 132.2, 128.9 (q, C−F, $^2J_{C-F}$ = 32.4 Hz), 128.3, 127.6, 126.6, 125.1, 124.4 (q, $^3J_{C-F}$ = 3.8 Hz), 121.7 (q, C−F,$^1J_{C-F}$ = 270.4 Hz), 70.5 37.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.4. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{15}H_{12}F_3Se$, 329.0051; found, 329.0045.

1-(4-Nitrophenyl)-2-(phenylselanyl)ethan-1-ol (3n). Compound **3n** was prepared according to the general procedure and isolated as an oil (65 mg, 81% yield) after flash chromatography (petroleum ether/ethyl acetate = 8:1). ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.7 Hz, 2H), 7.50−7.42 (m, 2H), 7.39 (d, J = 8.7 Hz, 2H), 7.21−7.17 (m, 3H), 4.73 (dt, J = 9.2, 3.2 Hz, 1H), 3.20 (dd, J = 13.0, 3.9 Hz, 1H), 3.12 (d, J = 2.7 Hz, 2H), 2.98 (dd, J = 13.0, 9.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 148.6, 146.3, 132.3, 128.4, 127.3, 126.8, 125.6, 122.6, 70.16, 37.15. Spectral data are in agreement with literature values.[39]

1-(2-Chlorophenyl)-2-(phenylselanyl)ethan-1-ol (3o). Compound **3o** was prepared according to the general procedure and isolated as an oil (72 mg, 93% yield) after flash chromatography (petroleum ether/ethyl acetate = 25:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, J = 8.1, 1.7 Hz, 1H), 7.51−7.46 (m, 2H), 7.20−7.17 (m, 5H), 7.14−7.06 (m, 1H), 5.02 (dt, J = 9.6, 2.9 Hz, 1H), 3.37 (dd, J = 12.9, 3.0 Hz, 1H), 2.95 (d, J = 3.0 Hz, 1H), 2.86 (dd, J = 12.9, 9.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 138.7, 132.1, 130.5, 128.3, 128.1, 127.7, 127.6, 126.4, 126.1, 126.0, 67.6, 35.5. Spectral data are in agreement with literature values.[15a]

1-(3-Bromophenyl)-2-(phenylselanyl)ethan-1-ol (3p). Compound **3p** was prepared according to the general procedure and isolated as an oil (80 mg, 90% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46−7.40 (m, 2H), 7.3.8−7.37 (m, 1H), 7.28 (dt, J = 7.7, 1.6 Hz, 1H), 7.21−7.16 (m, 2H), 7.16−7.03 (m, 2H), 4.57 (dt, J = 9.3, 3.2 Hz, 1H), 3.14 (dd, J = 12.9, 3.7 Hz, 1H), 3.04−2.84 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 143.7, 132.2, 129.9, 129.0, 128.3, 127.9, 127.7, 126.5, 123.4, 121.6, 70.4, 37.2. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{14}H_{12}BrSe$ 338.9282; found, 338.9273.

1-(2,4-Dimethylphenyl)-2-(phenylselanyl)ethan-1-ol (3q). Compound **3q** was prepared according to the general procedure and isolated as an oil (68 mg, 89% yield) after flash chromatography (petroleum ether/ethyl acetate = 1:2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61−7.46 (m, 2H), 7.33 (d, J = 7.9 Hz, 1H), 7.24−7.17 (m, 3H), 7.04−6.92 (m, 1H), 6.85 (d, J = 1.8 Hz, 1H), 4.82 (dt, J = 9.8, 2.9 Hz, 1H), 3.16 (dd, J = 12.9, 3.2 Hz, 1H), 2.96 (dd, J = 12.8, 9.8 Hz, 1H), 2.65 (d, J = 2.5 Hz, 1H), 2.22 (s, 3H), 2.03 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 136.4, 136.2, 133.3, 132.4, 130.2, 128.2, 128.0, 126.5, 126.0, 124.1, 67.5, 36.4, 20.0, 17.7. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{16}H_{17}Se$ 289.0490; found, 289.0482.

***anti*-2-(Phenylselanyl)-1,2,3,4-tetrahydronaphthalen-1-ol (3r).** Compound **3r** was prepared according to the general procedure and isolated as an oil (61 mg, 81% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61−7.45 (m, 2H), 7.46−7.33 (m, 1H), 7.26−7.15 (m, 3H), 7.16−7.05 (m, 2H), 7.01−6.83 (m, 1H), 4.59 (dd, J = 7.8, 3.4 Hz, 1H), 3.37 (ddd, J = 10.6, 7.7, 3.2 Hz, 1H), 2.96−2.54 (m, 3H), 2.31 (dtd, J = 14.2, 5.6, 3.2 Hz, 1H), 1.90−1.80 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 135.8, 134.54, 134.50, 128.1, 127.5, 127.2, 127.0, 126.6, 126.0, 125.4, 71.0, 47.6, 27.7, 26.5. Spectral data are in agreement with literature values.[40]

***anti*-2-(Phenylselanyl)-2,3-dihydro-1H-inden-1-ol (3s).** Compound **3s** was prepared according to the general procedure and isolated as a white solid (62 mg, 86% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). Mp: 93−94 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, J = 6.4, 3.0 Hz, 2H), 7.34−7.24 (m, 1H), 7.25−7.18 (m, 3H), 7.19−7.13 (m, 2H), 7.12−7.07 (m, 1H), 5.08 (t, J = 5.2 Hz, 1H), 3.67 (td, J = 7.7, 6.0 Hz, 1H), 3.35 (dd, J = 16.3, 7.8 Hz, 1H), 2.86 (dd, J = 16.3, 7.6 Hz, 1H), 2.28 (d, J = 5.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 142.0, 140.0, 133.6, 128.2, 127.6, 127.5, 126.7, 126.2, 123.5, 123.2, 80.4, 48.3, 36.6. Spectral data are in agreement with literature values.[40]

1-(Naphthalen-2-yl)-2-(phenylselanyl)ethan-1-ol (3t). Compound **3t** was prepared according to the general procedure and isolated as a white solid (74 mg, 91% yield) after flash chromatography (petroleum ether/ethyl acetate = 17:1). Mp: 52−53 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77−7.57 (m, 4H), 7.51−7.39 (m, 2H), 7.38−7.31 (m, 2H), 7.29 (dd, J = 8.5, 1.8 Hz, 1H), 7.20−7.09 (m, 3H), 4.77 (dt, J = 9.2, 3.1 Hz, 1H), 3.23 (dd, J = 12.8, 3.8 Hz, 1H), 3.08 (dd, J = 12.8, 9.3 Hz, 1H), 2.96 (d, J = 2.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 138.8, 132.1, 132.1, 132.0, 128.2, 128.1, 127.3, 126.9, 126.6, 126.3, 125.1, 124.9, 123.6, 122.7, 71.3 37.2. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{18}H_{15}Se$, 311.0333; found, 311.0327.

2-(Phenylselanyl)-1-(pyridin-4-yl)ethan-1-ol (3u). Compound **3u** was prepared according to the general procedure and isolated as an oil (54 mg, 77% yield) after flash chromatography (petroleum ether/ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$): δ 8.54−8.31 (m, 2H), 7.64−7.37 (m, 2H), 7.32−7.10 (m, 5H), 4.65 (dd, J = 9.2, 3.7 Hz, 1H), 3.23 (dd, J = 12.9, 3.7 Hz, 1H), 2.99 (dd, J = 12.9, 9.2 Hz, 1H), 2.57 (brs, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.5, 148.7, 132.44, 132.39, 128.4, 127.5, 126.8, 119.8, 69.6, 37.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{14}NOSe$, 280.0235; found, 280.0235.

1-(4-Methylthiazol-5-yl)-2-(phenylselanyl)ethan-1-ol (3v). Compound **3v** was prepared according to the general procedure and isolated as an oil (69 mg, 93% yield) after flash chromatography (petroleum ether/ethyl acetate = 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.45−7.36 (m, 2H), 7.25−7.15 (m, 3H), 4.95 (dd, J = 8.0, 5.3 Hz, 1H), 4.31 (brs, 1H), 3.44−2.91 (m, 2H), 2.15 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.0, 147.5, 133.5, 132.1, 128.3, 127.9, 126.5, 65.2, 36.5, 14.1. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{12}H_{14}NOSSe$, 299.9956; found, 299.9950.

2-(Phenylselanyl)-1-(thiophen-2-yl)ethan-1-ol (3w). Compound **3w** was prepared according to the general procedure and isolated as an oil (59 mg, 84% yield) after flash chromatography (petroleum ether/ethyl acetate = 1:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.48−7.40 (m, 2H), 7.26−7.06 (m, 4H), 6.92−6.81 (m, 2H), 4.91 (dt, J = 7.9, 3.6 Hz, 1H), 3.26 (dd, J = 12.8, 4.3 Hz, 1H), 3.16 (dd, J = 12.8, 8.6 Hz, 1H), 2.99 (d, J = 3.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.2, 132.1, 128.2, 128.0, 126.4, 125.7, 123.8, 123.0, 67.5, 37.1. Spectral data are in agreement with literature values.[40]

1-Ferroceneyl-2-(phenylselanyl)ethan-1-ol (3x). Compound **3x** was prepared according to the general procedure and isolated as an oil (64 mg, 66% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.45 (m, 2H), 7.24−7.16 (m, 3H), 4.51−4.39 (m, 1H), 4.22−4.19 (m, 1H), 4.14−4.12 (m, 1H), 4.10 (s, 7H), 3.18 (dd, J = 12.5, 4.2 Hz, 1H), 3.09 (dd, J = 12.5, 8.5 Hz, 1H), 2.46 (d, J = 3.2 Hz, 1H). $^{13}C\{^1H\}$

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

NMR (100 MHz, $CDCl_3$): δ 131.8, 128.9, 128.1, 126.1, 90.6, 67.6, 67.4, 67.1, 67.0, 66.0, 64.6, 35.7. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{19}FeOSe$, 386.9945; found, 386.9890.

2-Phenyl-1-(phenylselanyl)propan-2-ol (3y). Compound **3y** was prepared according to the general procedure and isolated as a white solid (68 mg, 94% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). Mp: 88−89 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39−7.29 (m, 4H), 7.22−7.18 (m, 2H), 7.16−7.06 (m, 4H), 3.48 (d, J = 12.5 Hz, 1H), 3.22 (d, J = 12.5 Hz, 1H), 2.87 br(s, 1H), 1.52 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 145.3, 131.8, 129.5, 128.0, 127.2, 126.0, 123.7, 72.6, 44.1, 28.7. Spectral data are in agreement with literature values.[39]

1,1-Diphenyl-2-(phenylselanyl)ethan-1-ol (3z). Compound **3z** was prepared according to the general procedure and isolated as an oil (73 mg, 83% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.40 (m, 2H), 7.38−7.31 (m, 4H), 7.26−7.18 (m, 4H), 7.16−7.11 (m, 5H), 3.78 (s, 2H), 3.50 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 144.3, 132.0, 129.7, 128.1, 127.3, 126.3, 126.2, 125.0, 76.4, 43.6. Spectral data are in agreement with literature values.[41]

***threo*-1,2-Diphenyl-2-(phenylselanyl)ethan-1-ol (3aa).** Compound **3aa** was prepared according to the general procedure and isolated as an oil (49 mg, 55% yield) after flash chromatography (petroleum ether/ethyl acetate = 15:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.28 (m, 2H), 7.24−7.05 (m, 8H), 7.05−7.01 (m, 3H), 6.96−6.87 (m, 2H), 4.96 (dd, J = 8.8, 2.3 Hz, 1H), 4.40 (d, J = 8.8 Hz, 1H), 3.13 (d, J = 2.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 139.7, 138.8, 134.3, 127.9, 127.7, 127.4 127.1, 127.07, 127.03, 126.7, 126.0, 125.7, 75.5, 58.9. Spectral data are in agreement with literature values.[9a]

***erythro*-1-Phenyl-2-(phenylselanyl)propan-1-ol (3ab).** Compound **3ab** was prepared according to the general procedure and isolated as an oil (65 mg, 90% yield) after flash chromatography (petroleum ether/ethyl acetate = 25:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.55−7.46 (m, 2H), 7.26−7.09 (m, 8H), 4.68 (t, J = 3.0 Hz, 1H), 3.53 (qd, J = 7.2, 3.3 Hz, 1H), 2.69 (d, J = 3.0 Hz, 1H), 1.14 (d, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 139.9, 133.7, 128.2 127.7, 127.1, 126.8, 126.4, 125.0, 73.3, 46.9, 13.0. Spectral data are in agreement with literature values.[42]

***anti*-2-(Phenylselanyl)cyclohexan-1-ol (3ac).** Compound **3ac** was prepared according to the general procedure and isolated as an oil (61 mg, 96% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.60−7.43 (m, 2H), 7.31−7.12 (m, 3H), 3.25 (tdd, J = 10.3, 4.3, 1.4 Hz, 1H), 2.90 (s, 1H), 2.82 (ddd, J = 12.3, 10.0, 4.0 Hz, 1H), 2.23−1.96 (m, 1H), 1.67−1.62 (m, 1H), 1.58−1.52 (m, 1H), 1.44−1.02 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 135.1, 128.0, 127.1, 125.5, 71.2, 52.5, 32.8, 32.3, 25.8, 23.4. Spectral data are in agreement with literature values.[22]

***anti*-2-(Phenylselanyl)cyclooctan-1-ol (3ad).** Compound **3ad** was prepared according to the general procedure and isolated as an oil (58 mg, 82% yield) after flash chromatography (petroleum ether/ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.60−7.41 (m, 2H), 7.27−7.12 (m, 3H), 3.61 (dd, J = 10.1, 4.6 Hz, 1H), 3.24 (ddd, J = 10.4, 8.5, 2.7 Hz, 1H), 2.87 (s, 1H), 2.22−2.14 (m, 1H), 1.95−1.71 (m, 2H), 1.70−1.58 (m, 3H), 1.54−1.38 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 134.4, 128.0, 126.9, 126.8, 72.6, 54.2, 30.9, 30.6, 25.8, 25.7, 24.2, 22.6. Spectral data are in agreement with literature values.[11a]

1-Methyl-2-(phenylselanyl)cyclohexan-1-ol (3ae). Compound **3ae** was prepared according to the general procedure and isolated as an oil (61 mg, 90% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.73−7.48 (m, 2H), 7.24−7.17 (m, 3H), 3.13 (dd, J = 12.3, 4.2 Hz, 1H), 2.58 (brs, 1H), 2.29−1.97 (m, 1H), 1.90−1.77 (m, 1H), 1.72−1.54 (m, 3H), 1.48−1.30 (m, 2H), 1.21 (s, 3H), 1.20−1.10 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 134.3, 130.0, 129.1, 127.5, 72.7, 60.2, 39.5, 33.4, 27.0, 24.0, 23.4. Spectral data are in agreement with literature values.[18c]

***threo*-4-(Phenylselanyl)hexan-3-ol (3af).** Compound **3af** was prepared according to the general procedure and isolated as an oil (60 mg, 94% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.72−7.41 (m, 2H), 7.34−6.89 (m, 3H), 3.42 (dt, J = 9.1, 4.7 Hz, 1H), 2.97 (dt, J = 9.1, 5.2 Hz, 1H), 2.45 (s, 1H), 1.80−1.71 (m, 1H), 1.67−1.39 (m, 3H), 1.02 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 133.8, 128.0, 127.9, 126.5, 73.3, 57.1, 26.7, 24.6, 12.0, 9.2. Spectral data are in agreement with literature values.[43]

2,3-Dimethyl-3-(phenylselanyl)butan-2-ol (3ag). Compound **3ag** was prepared according to the general procedure and isolated as an oil (48 mg, 75% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.66−7.50 (m, 2H), 7.37−7.25 (m, 1H), 7.24−7.16 (m, 2H), 2.31 (s, 1H), 1.33 (s, 6H), 1.27 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 137.5, 127.7, 127.6, 127.0, 74.8, 58.8, 25.6, 24.8. Spectral data are in agreement with literature values.[18c]

1-(Phenylselanyl)octan-2-ol (3ah). Compound **3ah** was prepared according to the general procedure and isolated as an oil (38 mg, 53% yield) after flash chromatography (petroleum ether/ethyl acetate = 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.47−7.44 (m, 2H), 7.20−7.18 (m, 3H), 3.59 (dq, J = 5.9, 2.8 Hz, 1H), 3.07 (dd, J = 12.7, 3.5 Hz, 1H), 2.80 (dd, J = 12.7, 8.6 Hz, 1H), 2.35 (d, J = 3.6 Hz, 1H), 1.49−1.41 (m, 2H), 1.40−1.29 (m, 1H), 1.20−1.17 (m, 7H), 0.79 (t, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 132.0, 128.3, 128.2, 126.2, 68.8, 36.2, 35.6, 30.7, 28.2, 24.7, 21.6, 13.1. Spectral data are in agreement with literature values.[14]

2-(Phenylselanyl)octan-1-ol (3ah′). Compound **3ah′** was prepared according to the general procedure and isolated as an oil (22 mg, 31% yield) after flash chromatography (petroleum ether/ethyl acetate = 40:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.56−7.39 (m, 2H), 7.30−7.11 (m, 3H), 3.55 (d, J = 12.0 Hz, 1H), 3.45 (dd, J = 11.6, 6.8 Hz, 1H), 3.16 (dtd, J = 7.6, 6.4, 5.0 Hz, 1H), 2.17 (s, 1H), 1.64−1.44 (m, 5H), 1.42−1.14 (m, 5H), 0.79 (t, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 134.4, 128.1, 126.9, 126.4, 63.2, 49.6, 30.7, 30.6, 28.0, 26.8, 21.6, 13.1. Spectral data are in agreement with literature values.[14]

(8*R*,9*S*,13*S*,14*S*)-3-(1-Hydroxy-2-(phenylselanyl)ethyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (3ai). Compound **3ai** was prepared according to the general procedure and isolated as an oil (84 mg, 74% yield) after flash chromatography (petroleum ether/ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, J = 6.6, 2.9 Hz, 2H), 7.26−7.15 (m, 4H), 7.09−6.98 (m, 2H), 4.63 (dt, J = 9.2, 2.9 Hz, 1H), 3.22 (dd, J = 12.8, 3.8 Hz, 1H), 3.07 (dd, J = 12.7, 9.4 Hz, 1H), 2.82 (dd, J = 9.3, 4.3 Hz, 2H), 2.74 (brs, 1H), 2.43 (dd, J = 18.8, 8.7 Hz, 1H), 2.33 (dd, J = 10.0, 4.5 Hz, 1H), 2.26−2.17 (m, 1H), 2.12−1.85 (m, 4H), 1.60−1.50 (m, 2H), 1.49−1.35 (m, 4H), 0.83 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 220.1, 138.9, 138.5, 138.4, 135.7, 132.0, 128.2, 126.3, 125.3, 124.5, 122.3, 71.0, 49.4, 46.9, 43.3, 37.2, 37.0, 34.8, 30.5, 28.4, 25.4, 24.7, 20.5, 12.8. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{26}H_{29}OSe$, 437.1378; found, 437.1370.

7-(1-Hydroxy-2-(phenylselanyl)ethyl)-2*H*-chromen-2-one (3aj). Compound **3aj** was prepared according to the general procedure and isolated as a yellow solid (70 mg, 81% yield) after flash chromatography (petroleum ether/ethyl acetate = 3:1). Mp: 77−79 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 9.5 Hz, 1H), 7.45 (dd, J = 6.6, 3.0 Hz, 2H), 7.34 (d, J = 7.9 Hz, 1H), 7.26−7.10 (m, 5H), 6.30 (d, J = 9.5 Hz, 1H), 4.73 (d, J = 7 Hz, 1H), 3.22 (dd, J = 12.9, 4.0 Hz, 1H), 3.17 (brs, 1H), 3.03 (dd, J = 12.9, 8.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 159.8, 153.0, 146.2, 142.1, 132.2, 128.3, 127.6, 126.9, 126.6, 121.0, 117.2, 115.4, 113.2, 70.4, 37.1. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{15}O_3Se$. 347.0181; found, 347.0176.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-(1-Hydroxy-2-(phenylselanyl)ethyl)benzoate (3ak). Compound **3ak** was prepared according to the general procedure and isolated as an oil (103 mg, 90% yield) after flash chromatography (petroleum ether/ethyl acetate = 18:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 8.3 Hz, 2H), 7.56−7.37 (m, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.26−7.14 (m,

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

3H), 4.84 (td, J = 10.9, 4.4 Hz, 1H), 4.70 (dt, J = 9.1, 3.3 Hz, 1H), 3.20 (dd, J = 12.8, 3.8 Hz, 1H), 3.10−2.92 (m, 2H), 2.03 (dd, J = 12.0, 4.3 Hz, 1H), 1.93−1.81 (m, 1H), 1.64 (dt, J = 11.9, 2.8 Hz, 2H), 1.52−1.41 (m, 2H), 1.12−0.96 (m, 2H), 0.85 (d, J = 4.9 Hz, 3H), 0.83 (d, J = 5.2 Hz, 3H), 0.80−0.76 (m, 1H), 0.70 (d, J = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.8, 146.3, 132.2, 129.2, 128.8, 128.3, 127.8, 126.5, 124.7, 73.8, 70.7, 46.2, 39.9, 37.2, 33.3, 30.4, 25.4, 22.6, 21.0, 19.7, 15.5. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{25}H_{33}O_3Se$, 461.1589; found, 461.1577.

((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-Tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4′,5′-*d*]pyran-5-yl)methyl 4-(1-Hydroxy-2-(phenylselanyl)ethyl)benzoate (3al). Compound **3al** was prepared according to the general procedure and isolated as a white solid (84 mg, 60% yield) after flash chromatography (petroleum ether/ethyl acetate = 5:1). Mp: 35−36 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 8.3 Hz, 2H), 7.60−7.45 (m, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.27−7.14 (m, 3H), 5.49 (d, J = 5.0 Hz, 1H), 4.70 (dd, J = 9.4, 3.6 Hz, 1H), 4.58 (dd, J = 7.9, 2.5 Hz, 1H), 4.45 (dd, J = 11.5, 4.8 Hz, 1H), 4.35 (dd, J = 11.5, 7.6 Hz, 1H), 4.28 (dd, J = 5.1, 2.6 Hz, 1H), 4.25 (dd, J = 7.9, 1.9 Hz, 1H), 4.10 (ddd, J = 7.1, 4.7, 1.8 Hz, 1H), 3.22 (dd, J = 12.9, 3.7 Hz, 1H), 3.01 (dd, J = 12.8, 9.4 Hz, 1H), 2.91 (brs, 1H), 1.44 (s, 3H), 1.41 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.1, 146.5, 132.3, 129.0, 128.5, 128.3, 127.7, 126.6, 124.7, 108.7, 107.8, 95.3, 70.6, 70.1, 69.7, 69.5, 65.1, 62.9, 37.4, 25.0, 24.9, 24.0, 23.5. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{33}O_8Se$, 565.1335; found, 565.1327.

4-(1-Hydroxy-2-(phenylselanyl)ethyl)phenyl (2*S*)-2-(6-Methoxynaphthalen-2-yl)propanoate (3am). Compound **3am** was prepared according to the general procedure and isolated as an oil (90 mg, 71% yield) after flash chromatography (petroleum ether/ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.77−7.58 (m, 3H), 7.51−7.34 (m, 3H), 7.26−7.14 (m, 5H), 7.16−7.05 (m, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.62 (dd, J = 9.4, 3.5 Hz, 1H), 4.01 (q, J = 7.1 Hz, 1H), 3.85 (s, 3H), 3.17 (dd, J = 12.8, 3.7 Hz, 1H), 2.99 (dd, J = 12.8, 9.4 Hz, 1H), 2.74 (brs, 1H), 1.61 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.1, 156.7, 149.3, 138.9, 134.0, 132.8, 132.1, 128.28, 128.25, 127.92, 127.88, 126.4, 126.3, 125.8, 125.10, 125.05, 120.4, 118.1, 104.5, 70.6, 54.3, 44.5, 37.4, 17.5. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{28}H_{25}O_3Se$, 489.0963; found, 489.0953.

7-(1-Hydroxy-2-(phenylselanyl)ethyl)-3-(4-methoxyphenyl)-4*H*-chromen-4-one (3an). Compound **3an** was prepared according to the general procedure and isolated as a white solid (104 mg, 92% yield) after flash chromatography (petroleum ether/ethyl acetate = 3:1). Mp: 114−116 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 8.2 Hz, 1H), 7.86 (s, 1H), 7.54−7.29 (m, 5H), 7.22−7.08 (m, 4H), 6.87 (d, J = 8.8 Hz, 2H), 4.74 (dd, J = 8.9, 3.9 Hz, 1H), 3.74 (s, 3H), 3.40 (d, J = 3.6 Hz, 1H), 3.22 (dd, J = 12.8, 4.0 Hz, 1H), 3.03 (dd, J = 12.8, 8.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 175.2, 158.6, 155.1, 151.6, 148.1, 132.2, 129.0, 128.3, 127.7, 126.5, 125.5, 123.9, 122.9, 122.6, 121.8, 114.1, 112.9, 70.4, 54.3, 36.9. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{21}O_4Se$, 453.0600; found, 453.0593.

4-(1-Hydroxy-2-(phenylselanyl)ethyl)phenyl (tert-butoxycarbonyl)-L-valinate (3ao). Compound **3ao** was prepared according to the general procedure and isolated as an oil (98 mg, 80% yield) after flash chromatography (petroleum ether/ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50−7.38 (m, 2H), 7.27 (d, J = 8.7 Hz, 2H), 7.23−7.14 (m, 3H), 6.97 (d, J = 8.6 Hz, 2H), 5.04 (d, J = 9.1 Hz, 1H), 4.66 (dd, J = 9.5, 3.6 Hz, 1H), 4.37 (dd, J = 9.1, 4.7 Hz, 1H), 3.19 (dd, J = 12.8, 3.8 Hz, 1H), 3.02 (dd, J = 12.8, 9.3 Hz, 1H), 2.94 (brs, 1H), 2.39−2.17 (m, 1H), 1.39 (s, 9H), 0.99 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.1, 154.7, 148.9, 139.4, 132.1, 128.3 128.0, 126.4, 126.0, 120.4, 79.0, 70.6, 57.6, 37.3, 30.3, 27.3, 18.1, 16.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_5Se$, 494.1440; found, 494.1429.

1-((*R*)-2,8-Dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)-chroman-6-yl)-2-(phenylselanyl)ethan-1-ol (3ap). Compound **3ap** was prepared according to the general procedure and isolated as an oil (92 mg, 63% yield) after flash chromatography (petroleum ether/ethyl acetate = 5:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.55−7.44 (m, 2H), 7.25−6.95 (m, 3H), 6.89−6.75 (m, 2H), 4.56 (dt, J = 9.4, 2.9 Hz, 1H), 3.21 (dd, J = 12.7, 3.7 Hz, 1H), 3.09 (dd, J = 12.7, 9.5 Hz, 1H), 2.82−2.49 (m, 3H), 2.07 (s, 3H), 1.69 (dt, J = 16.1, 6.7 Hz, 2H), 1.58−1.42 (m, 8H), 1.42−1.17 (m, 10H), 1.10−0.95 (m, 6H), 0.87−0.77 (m, 12H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.9, 132.0, 131.4, 128.4, 128.1, 126.2, 125.4, 124.9, 123.4, 119.4, 75.1, 71.2, 39.2, 39.1, 38.3, 37.2, 36.4, 36.4, 36.3, 31.8, 31.6, 30.1, 28.7, 27.0, 23.8, 23.4, 23.3, 23.2, 21.7, 21.6, 21.3, 20.0, 18.7, 18.6, 15.1. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{35}H_{53}OSe$, 569.3256; found, 569.3248.

4-(4-(1-Hydroxy-2-(phenylselanyl)ethyl)-3-methoxyphenyl)butan-2-one (3aq). Compound **3aq** was prepared according to the general procedure and isolated as an oil (60 mg, 64% yield) after flash chromatography (petroleum ether/ethyl acetate = 4:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.53−7.35 (m, 2H), 7.24 (d, J = 7.7 Hz, 1H), 7.21−7.10 (m, 3H), 6.70 (dd, J = 7.7, 1.5 Hz, 1H), 6.59 (d, J = 1.5 Hz, 1H), 4.92 (dt, J = 9.0, 4.5 Hz, 1H), 3.71 (s, 3H), 3.35 (dd, J = 12.6, 4.0 Hz, 1H), 3.05 (dd, J = 12.7, 8.9 Hz, 1H), 2.95 (d, J = 5.2 Hz, 1H), 2.80 (t, J = 7.8 Hz, 2H), 2.80 (t, J = 7.3 Hz, 2H), 2.07 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 206.9, 155.1, 140.9, 131.3, 128.9, 128.0, 127.2, 125.8, 125.7, 119.4, 109.6, 67.9, 54.1, 44.1, 35.0, 29.1, 28.7. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{19}H_{21}O_2Se$, 361.0701; found, 361.0694.

2-(Methylselanyl)-1-phenylethan-1-ol (4a). Compound **4a** was prepared according to the general procedure and isolated as an oil (47 mg, 88% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 8.01−6.80 (m, 5H), 4.67 (ddd, J = 9.1, 4.1, 2.5 Hz, 1H), 2.97 (s, 1H), 2.83 (dd, J = 12.8, 4.2 Hz, 1H), 2.72 (dd, J = 12.8, 9.0 Hz, 1H), 1.87 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.7, 127.5, 126.8, 124.8, 71.0, 34.9, 3.6. Spectral data are in agreement with literature values.[44]

2-(Ethylselanyl)-1-phenylethan-1-ol (4b). Compound **4b** was prepared according to the general procedure and isolated as an oil (44 mg, 76% yield) after flash chromatography (petroleum ether/ethyl acetate = 30:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49−7.23 (m, 5H), 4.77 (dt, J = 9.1, 3.2 Hz, 1H), 3.00 (dd, J = 12.9, 3.9 Hz, 1H), 2.91 (d, J = 2.8 Hz, 1H), 2.82 (dd, J = 12.9, 9.2 Hz, 1H), 2.57 (q, J = 7.5 Hz, 2H), 1.40 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 142.8, 128.5, 127.8, 125.8, 72.3, 34.2, 17.9, 15.8. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{10}H_{13}Se$, 213.0177; found, 213.0173.

2-(Benzylselanyl)-1-phenylethan-1-ol (4c). Compound **4c** was prepared according to the general procedure and isolated as a white solid (55 mg, 75% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). Mp: 38−40 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45−7.02 (m, 10H), 4.55 (dt, J = 8.7, 3.4 Hz, 1H), 3.65 (s, 2H), 2.79−2.72 (m, 2H), 2.67 (dd, J = 13.1, 8.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.8, 137.8, 127.9, 127.6, 127.4, 126.8, 125.9, 124.7, 71.3, 33.1, 26.4. Spectral data are in agreement with literature values.[26]

2-(Cyclohexylselanyl)-1-phenylethan-1-ol (4d). Compound **4d** was prepared according to the general procedure and isolated as an oil (45 mg, 63% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.64−6.57 (m, 5H), 4.68 (dt, J = 9.2, 3.3 Hz, 1H), 2.95 (dd, J = 12.8, 3.9 Hz, 1H), 2.92 (d, J = 3.0 Hz, 1H), 2.84−2.79 (m, 1H), 2.75 (dd, J = 12.8, 9.1 Hz, 1H), 1.98−1.89 (m, 2H), 1.72−1.63 (m, 2H), 1.50−1.34 (m, 2H), 1.28−1.11 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 141.9, 127.4, 126.7, 124.79, 71.3, 38.4, 33.6, 33.6, 32.3, 25.78, 25.77, 24.7. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{14}H_{19}Se$, 267.0646; found, 267.0643.

2-((4-Methoxyphenyl)selanyl)-1-phenylethan-1-ol (4e). Compound **4e** was prepared according to the general procedure and isolated as an oil (54 mg, 70% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.7 Hz, 2H), 7.28−7.15 (m, 5H), 6.74 (d, J = 8.7 Hz, 2H), 4.58 (dd, J = 9.5, 3.6 Hz, 1H), 3.71 (s, 3H), 3.10 (dd, J = 12.7, 3.6 Hz, 1H), 2.94 (dd, J = 12.7, 9.6 Hz, 1H), 2.88 (s, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 158.5, 141.4, 134.9, 127.4, 126.8, 124.8, 117.7, 113.9, 70.9, 54.3, 38.5. HRMS (ESI): m/z $[M + H - H_2O]^+$ calcd for $C_{15}H_{15}OSe$ 291.0283; found, 291.0278.

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

2-((4-(*tert*-Butyl)phenyl)selanyl)-1-phenylethan-1-ol (4f). Compound **4f** was prepared according to the general procedure and isolated as an oil (67 mg, 81% yield) after flash chromatography (petroleum ether/ethyl acetate = 40:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.4 Hz, 2H), 7.31−7.16 (m, 7H), 4.67 (dd, J = 9.5, 3.6 Hz, 1H), 3.21 (dd, J = 12.8, 3.7 Hz, 1H), 3.03 (dd, J = 12.8, 9.5 Hz, 1H), 2.30 (s, 1H), 1.24 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.7, 141.5, 132.1, 127.5, 126.8, 125.4, 124.8, 124.3, 71.1, 37.6, 33.5, 30.2. HRMS (ESI): m/z [M + H − H_2O]$^+$ calcd for $C_{18}H_{21}Se$, 317.0803; found, 317.0797.

2-(Benzo[*d*][1,3]dioxol-5-ylselanyl)-1-phenylethan-1-ol (4g). Compound **4g** was prepared according to the general procedure and isolated as an oil (67 mg, 84% yield) after flash chromatography (petroleum ether/ethyl acetate = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.14 (m, 5H), 7.01 (dd, J = 7.9, 1.7 Hz, 1H), 6.98 (d, J = 1.6 Hz, 1H), 6.67 (d, J = 7.9 Hz, 1H), 5.91 (s, 2H), 4.64 (dd, J = 9.4, 3.6 Hz, 1H), 3.15 (dd, J = 12.7, 3.6 Hz, 1H), 2.99 (dd, J = 12.8, 9.5 Hz, 1H), 2.74 (d, J = 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 147.1, 146.8, 141.4, 127.5, 127.2, 126.9, 124.8, 118.8, 113.6, 108.2, 100.3, 71.0, 38.7. HRMS (ESI): m/z [M + H − H_2O]$^+$ calcd for $C_{15}H_{13}O_2Se$, 305.0075; found, 305.0070.

2-(Naphthalen-2-ylselanyl)-1-phenylethan-1-ol (4h). Compound **4h** was prepared according to the general procedure and isolated as an oil (61 mg, 75% yield) after flash chromatography (petroleum ether/ethyl acetate = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, J = 8.4 Hz, 1H), 7.85−7.65 (m, 3H), 7.47 (ddd, J = 19.3, 8.1, 6.8 Hz, 2H), 7.30 (dd, J = 8.2, 7.1 Hz, 1H), 7.27−7.08 (m, 5H), 4.73 (dt, J = 9.1, 3.2 Hz, 1H), 3.23 (dd, J = 12.6, 3.7 Hz, 1H), 3.11 (dd, J = 12.6, 9.4 Hz, 1H), 2.73 (d, J = 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.4, 133.2, 133.0, 132.2, 127.9, 127.7, 127.5, 127.2, 126.9, 126.6, 125.9, 125.3, 124.8, 124.7, 71.3, 37.4. Spectral data are in agreement with literature values.[45]

1-Phenyl-2-(thiophen-2-ylselanyl)ethan-1-ol (4i). Compound **4i** was prepared according to the general procedure and isolated as an oil (54 mg, 76% yield) after flash chromatography (petroleum ether/ethyl acetate = 15:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (dd, J = 5.3, 1.2 Hz, 1H), 7.28−7.17 (m, 5H), 7.15 (dd, J = 3.5, 1.2 Hz, 1H), 6.91 (dd, J = 5.3, 3.5 Hz, 1H), 4.69 (dd, J = 9.5, 3.7 Hz, 1H), 3.09 (dd, J = 12.6, 3.7 Hz, 1H), 2.95 (dd, J = 12.7, 9.4 Hz, 1H), 2.71 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.2, 134.9, 130.1, 127.5, 127.2, 126.9, 124.8, 121.6, 71.2, 40.4. HRMS (ESI): m/z [M + H − H_2O]$^+$ calcd for $C_{12}H_{11}SSe$, 266.9741; found, 266.9737.

(2-Methoxy-2-phenylethyl)(phenyl)selane (5a). Compound **5a** was prepared according to the general procedure and isolated as an oil (49 mg, 68% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.37 (m, 2H), 7.32−7.18 (m, 5H), 7.19−7.12 (m, 3H), 4.27 (dd, J = 8.5, 5.1 Hz, 1H), 3.25 (dd, J = 12.3, 8.5 Hz, 1H), 3.17 (s, 3H), 3.02 (dd, J = 12.3, 5.0 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.8, 131.5, 129.6, 128.0, 127.5, 127.1, 125.8, 125.6, 82.1, 56.0, 34.3. Spectral data are in agreement with literature values.[22]

(2-Ethoxy-2-phenylethyl)(phenyl)selane (5b). Compound **5b** was prepared according to the general procedure and isolated as an oil (55 mg, 72% yield) after flash chromatography (petroleum ether/ethyl acetate = 120:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−7.38 (m, 2H), 7.32−7.08 (m, 8H), 4.39 (dd, J = 8.5, 5.1 Hz, 1H), 3.50−3.18 (m, 3H), 3.02 (dd, J = 12.2, 5.1 Hz, 1H), 1.11 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.6, 131.5, 129.8, 127.9, 127.4, 126.9, 125.7, 125.5, 80.4, 63.6, 34.5, 14.2. Spectral data are in agreement with literature values.[22]

(2-Isopropoxy-2-phenylethyl)(phenyl)selane (5c). Compound **5c** was prepared according to the general procedure and isolated as a white solid (55 mg, 69% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). Mp: 44−46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.33 (m, 2H), 7.26−7.05 (m, 8H), 4.50 (dd, J = 8.8, 4.8 Hz, 1H), 3.42 (p, J = 6.1 Hz, 1H), 3.21 (dd, J = 12.1, 8.8 Hz, 1H), 2.98 (dd, J = 12.1, 4.7 Hz, 1H), 1.08 (d, J = 6.0 Hz, 3H), 0.99 (d, J = 6.2 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.4, 131.2, 130.0, 127.9, 127.4, 126.8, 125.53, 125.47, 77.7, 68.7, 35.0, 22.3, 20.3. Spectral data are in agreement with literature values.[21b]

(2-(Methoxy-d_3)-2-phenylethyl)(phenyl)selane (5d). Compound **5d** was prepared according to the general procedure and isolated as an oil (65 mg, 88% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.35 (m, 2H), 7.29−7.18 (m, 5H), 7.18−7.09 (m, 3H), 4.26 (dd, J = 8.5, 5.0 Hz, 1H), 3.24 (dd, J = 12.2, 8.4 Hz, 1H), 3.01 (dd, J = 12.2, 5.0 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.9, 131.5, 129.6, 128.0, 127.5, 127.0, 125.7, 125.6, 82.0, 55.5−54.7 (m), 34.3. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{15}H_{14}D_3OSe$, 296.0627; found, 296.0624.

Phenyl(2-phenyl-2-(2,2,2-trifluoroethoxy)ethyl)selane (5e). Compound **5e** was prepared according to the general procedure and isolated as an oil (52 mg, 58% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.39 (m, 2H), 7.32−7.21 (m, 5H), 7.20−7.14 (m, 3H), 4.52 (dd, J = 8.0, 5.4 Hz, 1H), 3.82−3.47 (m, 2H), 3.30 (dd, J = 12.7, 7.9 Hz, 1H), 3.05 (dd, J = 12.6, 5.4 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 138.2, 131.7, 129.2, 128.0, 127.8, 127.7, 126.0 (q, C−F, $^1J_{C-F}$ = 232.0 Hz), 126.0, 125.7, 82.0, 65.1 (q, C−F, $^2J_{C-F}$ = 34.3 Hz), 33.7. ^{19}F NMR(376 MHz, $CDCl_3$): δ −73.9. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{16}H_{16}F_3OSe$, 361.0313; found, 361.0324.

(2-Phenoxy-2-phenylethyl)(phenyl)selane (5f). Compound **5f** was prepared according to the general procedure and isolated as an oil (58 mg, 66% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.43 (m, 2H), 7.37−7.22 (m, 4H), 7.21−7.14 (m, 4H), 7.09 (dd, J = 8.7, 7.3 Hz, 2H), 6.80 (tt, J = 7.3, 1.1 Hz, 1H), 6.76−6.66 (m, 2H), 5.23 (dd, J = 8.3, 4.9 Hz, 1H), 3.43 (dd, J = 12.6, 8.2 Hz, 1H), 3.18 (dd, J = 12.6, 4.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.8, 139.6, 131.9, 129.3, 128.3, 128.0, 127.6, 127.0, 126.0, 125.1, 120.0, 115.0, 78.8, 34.6. Spectral data are in agreement with literature values.[46]

1-Phenyl-2-(phenylselanyl)ethyl Benzoate (5g). Compound **5g** was prepared according to the general procedure and isolated as an oil (65 mg, 68% yield) after flash chromatography (petroleum ether/ethyl acetate = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−7.81 (m, 2H), 7.55−7.39 (m, 3H), 7.35−7.30 (m, 4H), 7.31−7.21 (m, 3H), 7.17−7.10 (m, 3H), 6.09 (dd, J = 8.0, 5.7 Hz, 1H), 3.46 (dd, J = 12.9, 7.9 Hz, 1H), 3.29 (dd, J = 12.8, 5.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.5, 138.5, 132.1, 132.0, 128.9, 128.72, 128.70, 128.1, 127.5, 127.4, 127.3, 126.2, 125.5, 74.8, 32.6. Spectral data are in agreement with literature values.[21a]

4-Chloro-*N*-(1-phenyl-2-(phenylselanyl)ethyl)aniline (5h). Compound **5h** was prepared according to the general procedure and isolated as an oil (70 mg, 73% yield) after flash chromatography (petroleum ether/ethyl acetate = 150:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−7.33 (m, 2H), 7.29−7.10 (m, 8H), 6.90 (d, J = 8.8 Hz, 2H), 6.25 (d, J = 8.8 Hz, 2H), 4.39 (d, J = 3.8 Hz, 1H), 4.27 (dt, J = 8.6, 4.2 Hz, 1H), 3.25 (dd, J = 12.7, 4.4 Hz, 1H), 3.06 (dd, J = 12.7, 9.1 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.5, 141.1, 132.6, 128.3, 127.9, 127.83, 127.82, 126.26, 126.60, 125.2, 121.3, 113.7, 56.8, 35.3. Spectral data are in agreement with literature values.[47]

Phenyl(2-phenyl-2-(2,4,6-trimethoxyphenyl)ethyl)selane (9). Compound **9** was prepared according to the general procedure and isolated as an oil (28 mg, 26% yield) after flash chromatography (petroleum ether/ethyl acetate = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.33 (m, 2H), 7.28−7.22 (m, 2H), 7.17−7.10 (m, 5H), 7.09−6.99 (m, 1H), 6.02 (s, 2H), 4.85 (dd, J = 9.7, 7.0 Hz, 1H), 3.81 (dd, J = 3.9, 1.8 Hz, 1H), 3.71 (s, 3H), 3.68−3.63 (m, 7H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.8, 158.2, 143.2, 131.5, 130.3, 127.7, 126.84, 126.75, 125.3, 124.6, 111.3, 90.0, 54.6, 54.2, 39.1, 30.5. Spectral data are in agreement with literature values.[48]

Phenyl(2,4,6-trimethoxyphenyl)selane (10). Compound **10** was prepared according to the general procedure and isolated as a white solid (11 mg, 13% yield) after flash chromatography (petroleum ether/ethyl acetate = 25:1). Mp: 103−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−6.70 (m, 5H), 6.14 (s, 2H), 3.79 (s, 3H), 3.72 (s,

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 161.9, 160.9, 132.5, 127.7, 127.6, 124.2, 96.0, 90.1, 55.3, 54.4. Spectral data are in agreement with literature values.[32]

Gram-Scale Reaction for the Synthesis of β-Hydroxy Selenide 3a. To a 50 mL round-bottomed flask with a magnetic stir bar were added styrene (0.52 g, 5.00 mmol, 1.00 equiv), Ph_2Se_2 (1.56 g, 5.00 mmol, 1.00 equiv), PhIO (1.10 g, 5.00 mmol, 1.00 equiv), and 20 mL of CH_3CN/water (3:1). The reaction mixture was stirred overnight. The reaction was monitored by TLC. After completion of reaction, the mixture was added to 10 mL of H_2O and extracted with ethyl acetate (20 mL) three times. The combined organic layer was dried (Na_2SO_4) and concentrated to give a crude residue, which was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate = 15:1) to give **3a** in 82% yield (1.14 g).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00257.

Mechanistic studies, copies of NMR spectra for the obtained compounds, and X-ray crystallographic data of compounds **3s** (PDF)

Accession Codes

CCDC 2057938 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Authors

Gong-Qing Liu − *School of Pharmacy and Analysis & Testing Center, Nantong University, Nantong 226019, People's Republic of China*; orcid.org/0000-0002-8162-707X; Email: gqliu@ntu.edu.cn

Yong Ling − *School of Pharmacy and Analysis & Testing Center, Nantong University, Nantong 226019, People's Republic of China*; Email: Lyyyy111@sina.com

Authors

Zhi-Peng Liang − *School of Pharmacy and Analysis & Testing Center, Nantong University, Nantong 226019, People's Republic of China*

Wei Yi − *School of Pharmacy and Analysis & Testing Center, Nantong University, Nantong 226019, People's Republic of China*

Peng-Fei Wang − *School of Pharmacy and Analysis & Testing Center, Nantong University, Nantong 226019, People's Republic of China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00257

Author Contributions

†W.Y. and P.-F.W. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This study was supported by the Natural Science Foundation of Jiangsu Province (BK20170439) and Science and Technology Plan Projects of Nantong (JC2020072 and JC2019102).

■ REFERENCES

(1) For selected references, see: (a) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. Organoselenium and organotellurium compounds: toxicology and pharmacology. *Chem. Rev.* **2004**, *104*, 6255−6285. (b) Chen, Z.; Lai, H.; Hou, L.; Chen, T. Rational design and action mechanisms of chemically innovative organoselenium in cancer therapy. *Chem. Commun.* **2020**, *56*, 179−196. (c) Nicolaou, K. C.; Pastor, J.; Barluenga, S.; Winssinger, N. Polymer-supported selenium reagents for organic synthesis. *Chem. Commun.* **1998**, 1947−1948. (d) Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. Organoselenium Chemistry: Role of Intramolecular Interactions. *Chem. Rev.* **2010**, *110*, 4357−4416.

(2) Rigby, J. H.; Maharoof, U. S. M.; Mateo, M. E. Studies on the Narciclasine Alkaloids: Total Synthesis of (+)-Narciclasine and (+)-Pancratistatin. *J. Am. Chem. Soc.* **2000**, *122*, 6624−6628.

(3) Azuma, H.; Tamagaki, S.; Ogino, K. Stereospecific Total Syntheses of Sphingosine and Its Analogues from L-Serine. *J. Org. Chem.* **2000**, *65*, 3538−3541.

(4) Treadwell, E. M.; Neighbors, J. D.; Wiemer, D. F. A Cascade Cyclization Approach to Schweinfurthin B. *Org. Lett.* **2002**, *4*, 3639−3642.

(5) For selected examples, see: (a) Labar, D.; Dumont, W.; Hevesi, L.; Krief, A. Synthetic connective route to allyl alcohols from carbonyl compounds. *Tetrahedron Lett.* **1978**, *19*, 1145−1148. (b) Sharpless, K. B.; Lauer, R. F. Mild procedure for the conversion of epoxides to allylic alcohols. First organoselenium reagent. *J. Am. Chem. Soc.* **1973**, *95*, 2697−2699. (c) Hori, T.; Sharpless, K. B. Synthetic applications of arylselenenic and arylseleninic acids. Conversion of olefins to allylic alcohols and epoxides. *J. Org. Chem.* **1978**, *43*, 1689−1697.

(6) For selected examples, see: (a) Rémion, J.; Dumont, W.; Krief, A. New regiospecific routes to olefins from β-hydroxy selenides: - a stereospecific deoxygenation of epoxides - a [C,C] connective route to olefins. *Tetrahedron Lett.* **1976**, *17*, 1385−1388. (b) Reich, H. J.; Chow, F. Selenium stablized anions. Conversion of β-hydroxy selenides into olefins. *J. Chem. Soc., Chem. Commun.* **1975**, 790−791.

(7) For selected examples, see: (a) Dumont, W.; Van Ende, D.; Krief, A. β-hydroxy α-silyl selenides as versatile intermediates in organic synthesis. *Tetrahedron Lett.* **1979**, *20*, 485−488. (b) Reich, H. J.; Chow, F.; Shah, S. K. Selenium stabilized carbanions. Preparation of α-lithio selenides and applications to the synthesis of olefins by reductive elimination of β-hydroxy selenides and selenoxide syn elimination. *J. Am. Chem. Soc.* **1979**, *101*, 6638−6648.

(8) For selected examples, see: (a) Berlin, S.; Ericsson, C.; Engman, L. Construction of Tetrahydrofuran-3-ones from Readily Available Organochalcogen Precursors via Radical Carbonylation/Reductive Cyclization. *Org. Lett.* **2002**, *4*, 3−6. (b) Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. Ring-closure reactions through intramolecular displacement of the phenylselenonyl group by nitrogen nucleophiles: a new stereospecific synthesis of N-tosyl and N-benzoyl-1,3-oxazolidin-2-ones from β-hydroxyalkyl phenyl selenides. *Chem. - Eur. J.* **2004**, *10*, 1752−1764. (c) Tiecco, M.; Testaferri, L.; Marini, F.; Sternativo, S.; Santi, C.; Bagnoli, L.; Temperini, A. Intramolecular addition of carbon radicals to aldehydes: synthesis of enantiopure tetrahydrofuran-3-ols. *Tetrahedron* **2007**, *63*, 5482−5489.

(9) For selected examples, see: (a) Tiecco, M.; Testaferri, L.; Marini, F.; Sternativo, S.; Del Verme, F.; Santi, C.; Bagnoli, L.; Temperini, A. Synthesis of enantiomerically enriched β-hydroxy selenides by catalytic asymmetric ring opening of *meso*-epoxides with (phenylseleno)silanes. *Tetrahedron* **2008**, *64*, 3337−3342. (b) Detty, M. R. Phenylselenotrimethylsilane. A novel source of phenylselenide anion. *Tetrahedron Lett.* **1978**, *19*, 5087−5090. (c) Miyoshi, N.; Kondo, K.; Murai, S.; Sonoda, N. Synthesis of β-siloxyalkyl phenyl selenides by the reaction of phenyl trimethylsilyl selenide with epoxides. *Chem. Lett.* **1979**, *8*, 909−912.

(10) Kozikowski, A. P.; Ames, A. Dimethylaluminum methaneselenolate. A useful reagent for the preparation of selenoesters. A new

Friedel-Crafts acylation procedure promoted by copper(I). *Tetrahedron* **1985**, *41*, 4821−4834.
(11) For selected examples, see: (a) Movassagh, B.; Shamsipoor, M. Stereo- and Regioselective Zinc-Mediated Ring-Opening of Epoxides with Diselenides. *Synlett* **2005**, *2005*, 1316−1318. (b) Santi, C.; Santoro, S.; Battistelli, B.; Testaferri, L.; Tiecco, M. Preparation of the first bench-stable phenyl selenolate: an interesting "on water" nucleophilic reagent. *Eur. J. Org. Chem.* **2008**, *2008*, 5387−5390.
(12) Cravador, A.; Krief, A. Unusual reactivity of selenoboranes towards epoxides: new selective routes to β-hydroxyselenides and allyl alcohols. *Tetrahedron Lett.* **1981**, *22*, 2491−2494.
(13) For selected examples, see: (a) Posner, G. H.; Rogers, D. Z. Organic reactions at alumina surfaces. Mild and selective opening of epoxides by alcohols, thiols, benzeneselenol, amines, and acetic acid. *J. Am. Chem. Soc.* **1977**, *99*, 8208−8214. (b) Sun, J.; Yang, M.; Yuan, F.; Jia, X.; Yang, X.; Pan, Y.; Zhu, C. Catalytic Asymmetric Ring-Opening Reaction of *meso*-Epoxides with Aryl Selenols and Thiols Catalyzed by a Heterobimetallic Gallium-Titanium-Salen Complex. *Adv. Synth. Catal.* **2009**, *351*, 920−930. (c) Yang, M.; Zhu, C.; Yuan, F.; Huang, Y.; Pan, Y. Enantioselective ring-opening reaction of meso-epoxides with ArSeH catalyzed by heterometallic Ti-Ga-Salen system. *Org. Lett.* **2005**, *7*, 1927−1930.
(14) Nishiyama, Y.; Ohashi, H.; Itoh, K.; Sonoda, N. Activation of Sn-Se Bond: Regioselective Ring Opening Reaction of Epoxides with Tributylstannyl Phenylselenolate in the Presence of a Lewis Acid. *Chem. Lett.* **1998**, *27*, 159−160.
(15) For selected examples, see: (a) Min, L.; Wu, G.; Liu, M.; Gao, W.; Ding, J.; Chen, J.; Huang, X.; Wu, H. Copper-Catalyzed Oxirane-Opening Reaction with Aryl Iodides and Se Powder. *J. Org. Chem.* **2016**, *81*, 7584−7590. (b) Wu, G.; Min, L.; Li, H.; Gao, W.; Ding, J.; Huang, X.; Liu, M.; Wu, H. Metal-free synthesis of alkynyl alkyl selenides via three-component coupling of terminal alkynes, Se, and epoxides. *Green Chem.* **2018**, *20*, 1560−1563. (c) Leng, T.; Wu, G.; Zhou, Y.-B.; Gao, W.; Ding, J.; Huang, X.; Liu, M.; Wu, H. Silver-Catalyzed One-Pot Three-Component Selective Synthesis of β-Hydroxy Selenides. *Adv. Synth. Catal.* **2018**, *360*, 4336−4340.
(16) For selected examples, see: (a) Uemura, S.; Ohe, K.; Yamauchi, T.; Mizutaki, S.; Tamaki, K. Preparation of 2-arylpropanoic acids by oxidative aryl migration in (β-aryl-β-hydroxy)alkyl phenyl selenides. *J. Chem. Soc., Perkin Trans. 1* **1990**, *1*, 907−910. (b) Krief, A.; Dumont, W.; Clarembeau, M.; Bernard, G.; Badaoui, E. Synthesis of α-selenoalkyllithium compounds. *Tetrahedron* **1989**, *45*, 2005−2022. (c) Huang, X.; Duan, D.-H. A Novel Synthetic Approach to β-Arylselenenyl Tertiary Alcohols by the One-Pot Reaction of Chloromethyl Selenides and Ketones Promoted by Samarium Diiodide. *Synlett* **1998**, *1998*, 1191−1192. (d) Duan, D.-H.; Huang, X. The Reaction of the α-Selenium Stabilized Copper Reagents $ArSeCH_2Cu(CN)ZnCl$ with Aldehydes. *J. Chem. Res., Synop.* **1999**, 26−27. (e) Fernandopulle, S. C.; Clive, D. L. J.; Yu, M. [1-(Phenylseleno)alkyl]stannanes−Mixed Selenium/Tin Analogs of Acetals: Preparation from α-Hydroxystannanes and Use for Generating Selenium-Stabilized Carbanions. *J. Org. Chem.* **2008**, *73*, 6018−6021.
(17) For selected reviews, see: (a) Sun, K.; Wang, X.; Li, C.; Wang, H.; Li, L. Recent advances in tandem selenocyclization and tellurocyclization with alkenes and alkynes. *Org. Chem. Front.* **2020**, *7*, 3100−3119. (b) Santi, C.; Santoro, S.; Wiley-VCH Verlag GmbH & Co. KGaA, 2012; pp 1−51.
(18) For selected examples, see: (a) Clive, D. L. J. Reaction of olefins with benzeneselenenyl bromide and silver trifluoroacetate: a new method for access to the selenoxide fragmentation reaction. *J. Chem. Soc., Chem. Commun.* **1974**, 100−100. (b) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. Highly convenient method for hydroxyselenation of olefins. *J. Chem. Soc., Chem. Commun.* **1980**, 412−413. (c) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. Phenylselenenyl chloride in acetonitrile-water: A highly convenient reagent for hydroxyselenation of olefins and preparation of cyclic ethers from dienes. *Tetrahedron* **1985**, *41*, 5301−5306.
(19) For selected examples, see: (a) Toshimitsu, A.; Uemura, S.; Okano, M. Oxyselenation of olefins by the use of aryl or alkyl selenocyanates and copper or nickel halides. *J. Chem. Soc., Chem. Commun.* **1977**, 166−167. (b) Toshimitsu, A.; Aoai, T.; Uemura, S.; Okano, M. Facile oxyselenation of olefins in the presence of copper(II) or copper(I) chloride as catalyst. *J. Org. Chem.* **1980**, *45*, 1953−1958.
(20) For selected examples, see: (a) Nicolaou, K. C. Organoselenium-induced cyclizations in organic synthesis. *Tetrahedron* **1981**, *37*, 4097−4109. (b) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. N-Phenylselenophthalimide (N-PSP) and N-phenylselenosuccinimide (N-PSS). Two versatile carriers of the phenylseleno group. Oxyselenation of olefins and a selenium-based macrolide synthesis. *J. Am. Chem. Soc.* **1979**, *101*, 3704−3706.
(21) For selected examples, see: (a) Sun, L.; Yuan, Y.; Yao, M.; Wang, H.; Wang, D.; Gao, M.; Chen, Y.-H.; Lei, A. Electrochemical Aminoselenation and Oxyselenation of Styrenes with Hydrogen Evolution. *Org. Lett.* **2019**, *21*, 1297−1300. (b) Amri, N.; Wirth, T. Automated Electrochemical Selenenylations. *Synthesis* **2020**, *52*, 1751−1761. (c) Torii, S.; Uneyama, K.; Ono, M. A halide ion promoted electrochemical oxyselenenylation of olefins. *Tetrahedron Lett.* **1980**, *21*, 2741−2744.
(22) Perin, G.; Santoni, P.; Barcellos, A. M.; Nobre, P. C.; Jacob, R. G.; Lenardão, E. J.; Santi, C. Selenomethoxylation of Alkenes Promoted by Oxone®. *Eur. J. Org. Chem.* **2018**, *2018*, 1224−1229.
(23) Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. Oxidation of diphenyl diselenide with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). A new method for the electrophilic phenylselenenylation of alkenes under mild conditions. *Synlett* **2001**, *2001*, 1767−1771.
(24) (a) Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. Iodosobenzene diacetate and diphenyl diselenide: an electrophilic selenenylating agent of double bonds. *Synth. Commun.* **1998**, *28*, 1769−1778. (b) Tiecco, M.; Tingoli, M.; Testaferri, L. The use of selenium-containing intermediates to mediate or catalyze new organic reactions. *Pure Appl. Chem.* **1993**, *65*, 715−722. (c) Das, J. P.; Roy, U. K.; Roy, S. Synthesis of Alkynyl and Vinyl Selenides via Selenodecarboxylation of Arylpropiolic and Cinnamic Acids. *Organometallics* **2005**, *24*, 6136−6140. (d) Margarita, R.; Mercanti, C.; Parlanti, L.; Piancatelli, G. Hypervalent Iodine-Induced Multi-Component Reactions: Novel Thiocyano- and Isothiocyano-phenylselenenylating Reaction of Alkenes. *Eur. J. Org. Chem.* **2000**, *2000*, 1865−1870.
(25) Tiecco, M.; Testaferri, L.; Santi, C.; Marini, F.; Bagnoli, L.; Temperini, A.; Tomassini, C. Asymmetric selenohydroxylation of alkenes with camphorselenenyl sulfate. *Eur. J. Org. Chem.* **1998**, *1998*, 2275−2277.
(26) Zhang, Y.; Wu, S.; Yan, J. New Catalytic Method for the Synthesis of β-Hydroxy Selenides. *Helv. Chim. Acta* **2016**, *99*, 654−658.
(27) (a) Yi, W.; Wang, P.-F.; Lu, M.; Liu, Q.-Q.; Bai, X.; Chen, K.-D.; Zhang, J.-W.; Liu, G.-Q. Environmentally Friendly Protocol for the Oxidative Iodofunctionalization of Olefins in a Green Solvent. *ACS Sustainable Chem. Eng.* **2019**, *7*, 16777−16785. (b) Liu, G.-Q.; Li, Y.-M. Regioselective (Diacetoxyiodo)benzene-Promoted Halocyclization of Unfunctionalized Olefins. *J. Org. Chem.* **2014**, *79*, 10094−10109. (c) Liu, J.; Liu, Q.-Y.; Fang, X.-X.; Liu, G.-Q.; Ling, Y. Preparation of polysubstituted dihydrofurans through a $PhI(OAc)_2$-promoted haloenolcyclization of olefinic dicarbonyl compounds. *Org. Biomol. Chem.* **2018**, *16*, 7454−7460. (d) Yi, W.; Fang, X.-X.; Liu, Q.-Y.; Liu, G.-Q. Metal-Free Synthesis of Oxazolidine-2,4-diones and 3,3-Disubstituted Oxindoles via ICl-Induced Cyclization. *Eur. J. Org. Chem.* **2018**, *2018*, 6671−6681. (e) Yi, W.; Liu, Q.-Y.; Fang, X.-X.; Lou, S.-C.; Liu, G.-Q. Preparation of oxazolines and oxazoles via a $PhI(OAc)_2$-promoted cyclization of N-propargylamides. *Org. Biomol. Chem.* **2018**, *16*, 7012−7018.
(28) Reactions in other water-soluble solvents, such as acetone, DMF, and DMSO, are unable to give better results than in CH_3CN.

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304

(29) CCDC 2057938 (**3s**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk.
(30) Liao, M.-H.; Zhang, M.; Hu, D.-H.; Zhang, R.-H.; Zhao, Y.; Liu, S.-S.; Li, Y.-X.; Xiao, W.-L.; Tang, E. Controlling the selectivity of an intramolecular Friedel−Crafts alkylation with alkenes using selenium under mild conditions. *Org. Biomol. Chem.* **2020**, *18*, 4034−4045.
(31) (a) Freudendahl, D. M.; Santoro, S.; Shahzad, S. A.; Santi, C.; Wirth, T. Green chemistry with selenium reagents: development of efficient catalytic reactions. *Angew. Chem., Int. Ed.* **2009**, *48*, 8409−8411. (b) Santoro, S.; Santi, C.; Sabatini, M.; Testaferri, L.; Tiecco, M. Eco-friendly olefin dihydroxylation catalyzed by diphenyl diselenide. *Adv. Synth. Catal.* **2008**, *350*, 2881−2884. (c) Jing, X.; Yuan, D.; Yu, L. Green and Practical Oxidative Deoximation of Oximes to Ketones or Aldehydes with Hydrogen Peroxide/Air by Organoselenium Catalysis. *Adv. Synth. Catal.* **2017**, *359*, 1194−1201.
(32) Zhang, Q.-B.; Ban, Y.-L.; Yuan, P.-F.; Peng, S.-J.; Fang, J.-G.; Wu, L.-Z.; Liu, Q. Visible-light-mediated aerobic selenation of (hetero)arenes with diselenides. *Green Chem.* **2017**, *19*, 5559−5563.
(33) (a) Carmalt, C. J.; Crossley, J. G.; Knight, J. G.; Lightfoot, P.; Martín, A.; Muldowney, M. P.; Norman, N. C.; Orpen, A. G. An examination of the structures of iodosylbenzene (PhIO) and the related imido compound, $PhINSO_2$-4-Me-C_6H_4, by X-ray powder diffraction and EXAFS (extended X-ray absorption fine structure) spectroscopy. *J. Chem. Soc., Chem. Commun.* **1994**, *0*, 2367−2368. (b) Zhdankin, V. V.; Stang, P. J. Chemistry of Polyvalent Iodine. *Chem. Rev.* **2008**, *108*, 5299−5358.
(34) The proton of intermediate **11** might arise from the reaction solvent or adventitious H_2O in air.
(35) (a) Kice, J. L.; McAfee, F.; Slebocka-Tilk, H. The anhydride structure of several previously reported stable areneselenenic acids. *Tetrahedron Lett.* **1982**, *23*, 3323−3326. (b) Reich, H. J.; Willis, W. W., Jr.; Wollowitz, S. Stable selenenic acids. *Tetrahedron Lett.* **1982**, *23*, 3319−3322. (c) Kice, J. L.; McAfee, F.; Slebocka-Tilk, H. Mechanism of the hydrolysis of *o*-nitro- and *o*-benzoylbenzeneselenenic anhydrides. *J. Org. Chem.* **1984**, *49*, 3100−3106. (d) Kang, S. I.; Kice, J. L. The equilibrium between an areneselenenic acid and its anhydride. *J. Org. Chem.* **1985**, *50*, 2968−2972.
(36) (a) Davis, F. A.; Stringer, O. D.; Billmers, J. M. Oxidation of selenides to selenoxides using 2-sulfonyloxaziridines. *Tetrahedron Lett.* **1983**, *24*, 1213−1216. (b) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. Syn elimination of alkyl selenoxides. Side reactions involving selenenic acids. Structural and solvent effects of rates. *J. Org. Chem.* **1978**, *43*, 1697−1705.
(37) (a) Shi, M.; Wang, B.-Y.; Li, J. Reactions of gem-Aryl-Disubstituted Methylenecyclopropanes with Diaryl Diselenide in the Presence of Iodosobenzene Diacetate. *Eur. J. Org. Chem.* **2005**, *2005*, 759−765. (b) Yu, L.; Chen, B.; Huang, X. Multicomponent reactions of allenes, diaryl diselenides, and nucleophiles in the presence of iodosobenzene diacetate: direct synthesis of 3-functionalized-2-arylselenyl substituted allyl derivatives. *Tetrahedron Lett.* **2007**, *48*, 925−927. (c) Shahzad, S. A.; Venin, C.; Wirth, T. Diselenide- and Disulfide-Mediated Synthesis of Isocoumarins. *Eur. J. Org. Chem.* **2010**, *2010*, 3465−3472. (d) Jiang, M.; Shi, M. The reaction of mono-aryl substituted methylenecyclobutanes with diphenyl diselenide in the presence of iodosobenzene diacetate and H_2O. *Tetrahedron* **2009**, *65*, 798−801.
(38) Singh, D.; Deobald, A. M.; Camargo, L. R. S.; Tabarelli, G.; Rodrigues, O. E. D.; Braga, A. L. An Efficient One-Pot Synthesis of Symmetrical Diselenides or Ditellurides from Halides with CuO Nanopowder/Se^0 or Te^0/Base. *Org. Lett.* **2010**, *12*, 3288−3291.
(39) Wang, X.-L.; Li, H.-J.; Yan, J. Iodine-mediated regioselective hydroxyselenenylation of alkenes: Facile access to *β*-hydroxy selenides. *Chin. Chem. Lett.* **2018**, *29*, 479−481.
(40) Gruttadauria, M.; Meo, P. L.; Riela, S.; D′Anna, F.; Noto, R. Lipase-catalyzed resolution of *β*-hydroxy selenides. *Tetrahedron: Asymmetry* **2006**, *17*, 2713−2721.
(41) Movassagh, B.; Farshbaf, S. Regioselective Hydroxyselenation of Styrenes by Diselenides Using the $Zn/AlCl_3$ System. *Synthesis* **2010**, *2010*, 33−35.
(42) Aoki, I.; Nishibayashi, Y.; Uemura, S. Stereo- and chemoselectivity in reduction of *α*-[phenyl(or methyl)seleno]alkyl aryl ketones with metal hydrides. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 337−340.
(43) Gernigon, N.; Al-Zoubi, R. M.; Hall, D. G. Direct amidation of carboxylic acids catalyzed by ortho-iodo arylboronic acids: catalyst optimization, scope, and preliminary mechanistic study supporting a peculiar halogen acceleration effect. *J. Org. Chem.* **2012**, *77*, 8386−8400.
(44) Costa, C. E.; Clososki, G. C.; Barchesi, H. B.; Zanotto, S. P.; Nascimento, M. G.; Comasseto, J. V. Enzymatic resolution of (*RS*)-*β*-hydroxy selenides in organic media. *Tetrahedron: Asymmetry* **2004**, *15*, 3945−3954.
(45) Yang, M.-H.; Yuan, C.-Y.; Pan, Y.; Zhu, C.-J. Regioselective ring-opening reaction of 1,2-epoxides with arylselenol under solvent-free conditions and application to the synthesis of 1,3-oxazolidin-2-ones. *Chin. J. Chem.* **2006**, *24*, 669−673.
(46) Vieira, A. A.; Azeredo, J. B.; Godoi, M.; Santi, C.; da Silva Junior, E. N.; Braga, A. L. Catalytic Chalcogenylation under Greener Conditions: A Solvent-Free Sulfur- and Seleno-functionalization of Olefins via I_2/DMSO Oxidant System. *J. Org. Chem.* **2015**, *80*, 2120−2127.
(47) Huang, B.; Li, Y.; Yang, C.; Xia, W. Three-component aminoselenation of alkenes via visible-light enabled Fe-catalysis. *Green Chem.* **2020**, *22*, 2804−2809.
(48) Tang, E.; Zhao, Y.; Li, W.; Wang, W.; Zhang, M.; Dai, X. Catalytic Selenium-Promoted Intermolecular Friedel-Crafts Alkylation with Simple Alkenes. *Org. Lett.* **2016**, *18*, 912−915.

https://dx.doi.org/10.1021/acs.joc.1c00257
J. Org. Chem. 2021, 86, 5292−5304