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Copper-Catalyzed Oxirane-Opening Reaction with Aryl Iodides and Se Powder

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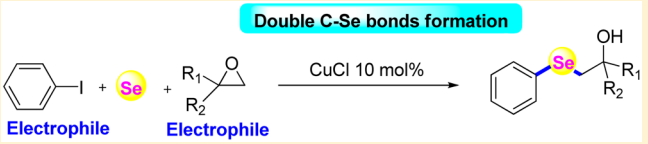
Supporting Information

ABSTRACT: Using Se powder as the selenating reagent, the copper-catalyzed double C−Se cross-coupling of aryl iodides, epoxides, and elemental selenium has been developed. This strategy provides a straightforward approach to the synthesis of β-hydroxy phenylselenides with excellent regioselectivity of the ring opening reaction. This process proceeds in generally good yields and is compatible with a broad range of functional groups.

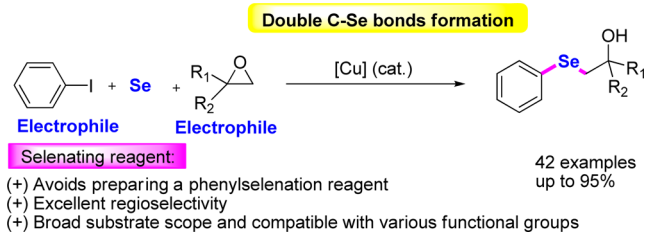


INTRODUCTION

Organoselenium chemistry has gained increasing attention because selenium-containing chemicals are prevalent in many drug candidates, biologically active compounds, functional organic materials, as well as in food chemistry.[1] Considering the significance of organoselenium compounds, especially β-hydroxy phenylselenides, these compounds are valuable intermediates in the synthesis of allylic alcohols,[2] olefins,[3] and vinyl selenides.[4] Therefore, the development of a new synthetic route for the introduction of stable, economical selenium reagent into organic skeletons would be of significant synthetic value.

In recent years, utilization of elemental selenium as a linkage atom has received considerable attention due to its commercial availability, stability, and easy handling as compared to those of commonly employed aryl selenium reagents. Unlike the use of diaryl diselenides, limited knowledge has been acquired when using transition metal-catalyzed transformation of selenium powder with aryl halides. This is likely due to the selenium having a high activation energy to destroy the structure of high polymer catenation and the proclivity of elemental selenium for transition metals to easily reinforce the stability of transition metal selenium clusters,[5] which attenuate the activity of catalysts. In 2005, Taniguchi[6] realized the first selenation of aryl iodides using aluminum as reductant and $MgCl_2$ as additive in combination with CuI/bpy to provide symmetrical diaryl selenides.[7] More recently, contributions have been extended to the synthesis of ebselen,[8] selenium-containing heterocycles,[9] and trifluoromethylselenolation.[10] Despite these encouraging advancements, achieving direct cross-coupling of elemental selenium in a general way remains a daunting challenge. Recently, our group has established the copper-catalyzed 3-phenylselenation of indoles through double C−Se bond formation of indoles with (hetero) aryl iodides and elemental selenium.[11] Inspired by this result, we envisioned that β-hydroxy phenylselenides, valuable synthetic intermediates of considerable interest in important natural compounds,[12] could be achieved by transition metal-catalyzed selenation of aryl halides with elemental selenium and, consequently, further react with epoxides to afford the corresponding product under certain reaction conditions (Scheme 1).

Scheme 1. Strategies for Cross-Coupling Reactions of Epoxides



Such a methodology would constitute an alternative to the common ring opening reactions of epoxides with selenolate anions.[13] The drawback of these reactions is the functional group tolerance and the loss of one equivalent of PhSe as waste. Clearly, such a single atom Se bridging different cross-coupling partners strategy will be widely accepted and used for complex pharmaceutical compound synthesis by synthetic chemists. Herein, we report the discovery of copper-catalyzed double C−Se bond formation that allows for regioselective ring opening of epoxides with (hetero) aryl iodides and elemental selenium.

RESULTS AND DISCUSSION

We commenced our study by examining the reaction between iodobenzene **1a** and 1,2-epoxycyclohexane **2a** in the presence of elemental selenium (Table 1). It is observed that three

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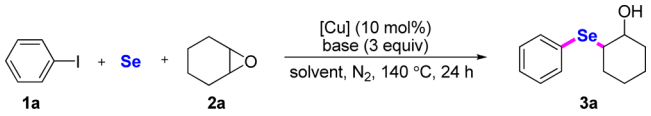
Table 1. Reaction Optimization[a]



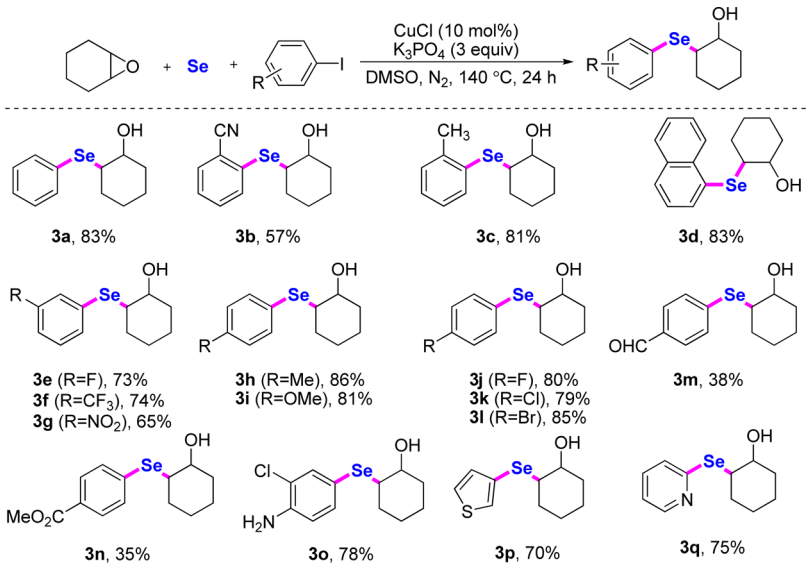
entry	[cat.]	base	solvent	yield %[b]
1	$Pd(OAc)_2$	K_3PO_4	DMSO	0
2	$Pd(PPh_3)_4$	K_3PO_4	DMSO	0
3	$Ni(acac)_2$	K_3PO_4	DMSO	0
4	$Ni(PPh_3)_2Cl_2$	K_3PO_4	DMSO	0
5	Cu	Cs_2CO_3	DMSO	32
6	Cu	Na_2CO_3	DMSO	0
7	Cu	K_2CO_3	DMSO	20
8	Cu	K_3PO_4	DMSO	45
9	Cu	KOH	DMSO	5
10	Cu	tBuOK	DMSO	4
11	CuO	K_3PO_4	DMSO	74
12	CuI	K_3PO_4	DMSO	64
13	CuBr	K_3PO_4	DMSO	76
14	CuCl	K_3PO_4	DMSO	83
15[c]	CuCl	K_3PO_4	DMSO	0
16[d]	CuCl	K_3PO_4	DMSO	33
17	$Cu(OAc)_2$	K_3PO_4	DMSO	70
18	$CuCl_2$	K_3PO_4	DMSO	79
19	CuCl	K_3PO_4	DMF	64
20	CuCl	K_3PO_4	HMPA	trace
21	CuCl	K_3PO_4	DCE	trace
22	CuCl	K_3PO_4	toluene	trace
23	CuCl	K_3PO_4	CH_3CN	trace
24[e]	CuCl	K_3PO_4	DMSO	45
25[f]	CuCl	K_3PO_4	DMSO	60

[a]Reaction conditions unless specified otherwise: iodobenzene (0.4 mmol), Se (0.8 mmol), cyclohexene oxide (1.2 mmol), [Cu] (0.04 mmol), base (1.2 mmol), solvent (2 mL), under N_2, 140 °C, 24 h. [b]Isolated yield. [c]Under O_2. [d]Under air. [e]At 90 °C. [f]At 110 °C.

critical reaction parameters have a remarkable effect on the reaction outcomes. First, in the examination of different transition metals, copper was found to be the only efficient catalyst species for this transformation (entries 1−5). We were pleased to find that the desired product was isolated in 45% yield under Cu as the catalyst with K_3PO_4 as the base in DMSO stirred at 140 °C for 24 h (entry 8). Different copper catalysts were screened, which showed that CuCl was the best choice (entry 14). Second, a strong base was necessary for the model reaction to occur, probably because bases were required to activate the selenium powder and therefore trigger the reaction. The effect of bases on the reaction was also observed to depend on the amounts of bases and their anions (entries 7−10). The best result was obtained when 3 equiv of K_3PO_4 was used (entry 8). Finally, the choice of a suitable solvent is critical for this transformation to be successful. When the reaction was conducted in polar solvent DMF, the starting material was not completely converted. No product was detected when apolar solvent toluene, DCE, or weak coordination CH_3CN were used instead of DMSO (entry 21−23). An N_2 atmosphere is essential for this reaction. No product was detected when the reaction was conducted under O_2, and air afforded a much lower 33% yield (entries 15 and 16, respectively). This is due to the fact that O_2 can intercept intermediates in the catalytic process. A control experiment showed that the copper catalyst is essential for this transformation, and no coupling product was detected in the absence of copper.

With the optimal conditions in hand, the scope of the reaction was explored. A wide range of aryl iodides were employed, and the reaction generally proceeds smoothly, affording the corresponding products in good to excellent yields (Scheme 2). When the iodobenzenes bearing a variety of electron-donating groups were used, such as methyl (**3c**, **3h**) and methoxy (**3i**), the highly reactive coupling partner gave a high yield. The reaction of iodobenzenes bearing electron-withdrawing groups, such as fluoro (**3e**, **3j**), chloro (**3k**), bromo (**3l**), cyan (**3b**), trifluoromethyl (**3f**), and nitro (**3g**), all gave the corresponding products in excellent yields. However, the

Scheme 2. Aryl Iodide Scope[a]



[a]Reaction conditions unless specified otherwise: aryl iodides (0.4 mmol), Se_8 (0.8 mmol), cyclohexene oxide (1.2 mmol), CuCl (0.04 mmol), K_3PO_4 (1.2 mmol), DMSO (2 mL), 140 °C, 24 h, N_2. Isolated yields are given.

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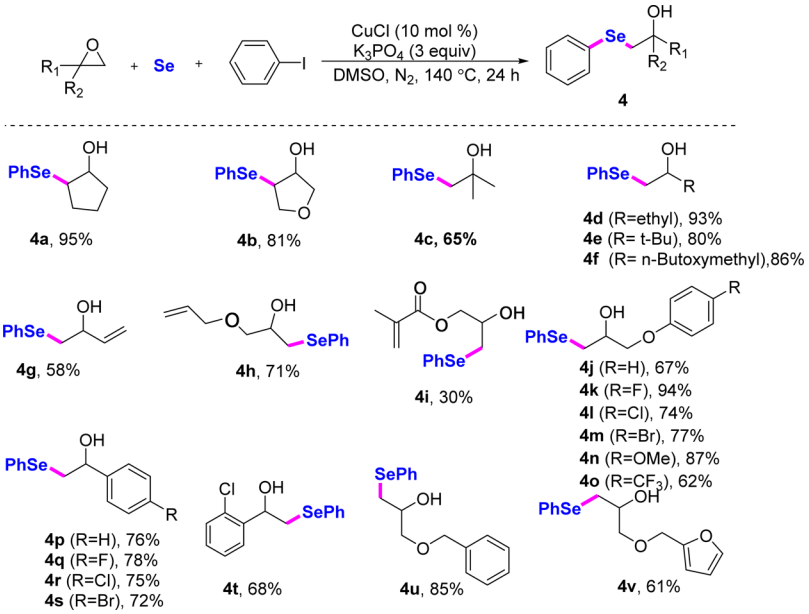
Scheme 3. Epoxides Scope[a]



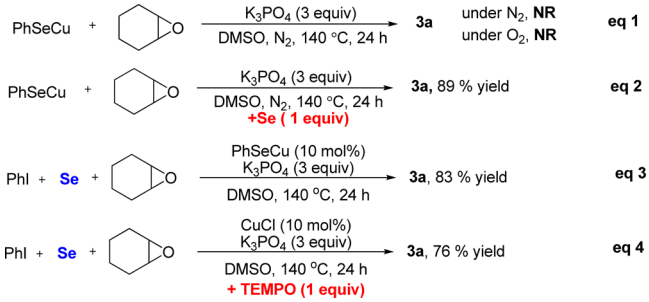
[a]Reaction conditions unless specified otherwise: iodobenzene (0.4 mmol), Se_8 (0.8 mmol), epoxides (1.2 mmol), CuCl (0.04 mmol), K_3PO_4 (1.2 mmol), DMSO (2 mL), 140 °C, 24 h, N_2. Isolated yields are given.

efficiency of this transformation was comparatively low when aldehyde and the ester group at the C4 position of iodobenzene afforded the corresponding product in 38 and 35% isolated yields, respectively. Most likely, the low electron density on the phenyl ring would reduce the tendency of C−I oxidative addition. The compatibility of these transformation groups in this reaction provided a platform for the further elaboration of the complex products. To our delight, substrates containing active hydrogen group amino (**3o**) could also be tolerated, which is a significant challenge in many coupling reactions. This is in sharp contrast to previous results[13] in which the phenylselenium nucleophilic reagents are very sensitive to these functional groups. Thus, the current reaction features the advantage of being versatile with operational simplicity. It is remarkable that heterocyclic iodides such as pyridine and thiophene are competent coupling partners and could also provide the corresponding products (**3p**, **3q**) in good yields.

Next, the scope of epoxides was further investigated under the optimized reaction conditions. As demonstrated in Scheme 3, the reaction worked well with region selectivity and excellent functional group tolerance. Cyclic epoxides (**4a**, **4b**) are efficiently opened to give the corresponding products in excellent yields. The reaction can be applied to the linear and branched aliphatic oxirane, which provided the products (**4c**−**f**) in good to excellent yields. Notably, double bond (**4g**, **4h**) and ester (**4i**) substituents could afford the desired products. We found that different electronic properties of substituents on the aromatic ring of 2-(phenoxymethyl)oxirane were compatible, such as methoxy (**4n**), fluoride (**4k**), chloride (**4l**), bromide (**4m**), and trifluoromethyl (**4o**); these functional groups have affected the substrates reactivity to a certain extent. Investigation of functionalized styrene oxides was highly indispensable, as the resulting α-hydroxy-2-phenylethyl phenyl selenides are a complement of the contrary products obtained by the previously reported methods that employed PhSeZnCl reagent as the coupling partner.[13e]

To understand the reaction mechanism, we conducted control experiments (Scheme 4). First, a stoichiometric

Scheme 4. Preliminary Mechanism Investigation



reaction of PhSeCu[6] with 1,2-epoxycyclohexane under either a N_2 or an O_2 atmosphere did not promote the reaction (Scheme 4, eq 1). An interesting phenomenon was observed; desired product **3a** was obtained in 89% isolated yield when 1 equiv of selenium powder was added under standard reaction conditions (eq 2). These experiments indicate that elemental selenium plays a critical role in the process of the oxirane opening reaction. Second, as shown in eq 3, PhSeCu may be a chemically competent intermediate produced in situ during the catalytic cycle. It could also rationalize why a small amount of diphenyl diselenides were detected in the reaction. Finally, when the radical inhibitor TEMPO was added to the reaction conditions, product **3a** was still obtained in 76% yield (eq 4), which suggested that a radical-involved mechanism could be ruled out. Although the details of the reaction mechanism remain unclear at the present time, we assume that the epoxide ring opening reaction is likely to involve an S_N2-type by the phenylselenium−copper complex intermediate generated in situ from the aryl iodide and elemental selenium.

In summary, we have demonstrated the synthesis of a broad range of β-hydroxy phenylselenides through a convergent

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three-component copper-catalyzed coupling approach. Commercially available, stable, easily handled elemental selenium was used as selenating reagent. The important feature of this method was its operational simplicity for applying it to broad substrate scopes. Further studies to develop related transformations and deeply understand the mechanism are underway.

EXPERIMENTAL SECTION

General Remarks. ^{1}H NMR (500 MHz), ^{13}C NMR (125 MHz), and ^{19}F NMR (470 MHz) spectra were recorded in $CDCl_3$ solutions using a 500 MHz spectrometer. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. All reactions were conducted using standard Schlenk techniques. Column chromatography was performed using EM silica gel 60 (300−400 mesh). ^{1}H NMR and ^{13}C NMR spectra are provided as Supporting Information. 4-Bromo styrene oxide,[14] 2-chloro styrene oxide,[14] 2-[(4-chlorophenoxy)methyl]oxirane,[14] 2-[(4-bromophenoxy)methyl]-oxirane,[14] 2-[(4-fluorophenoxy)methyl]oxirane,[14] 2-[(4-methoxyphenoxy)methyl]oxirane,[14] and 2-[(4-trifluoromethylphenoxy)methyl]oxirane[14] were prepared according to the reported procedures. ^{1}H and ^{13}C spectra of known compounds were in accordance with those described in the literature.

Procedure for Intermolecular Phenylselenation of Epoxide-Opening Reactions.[15] In a 25 mL Schlenk tube equipped with a stir bar were placed aryl iodides **1** (0.4 mmol), epoxides **2** (1.2 mmol), Se (0.8 mmol), CuCl (10 mol %), and K_3PO_4 (1.2 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 140 °C for 24 h. After it was cooled, the reaction mixture was diluted with 10 mL of ethyl ether and filtered through a pad of silica gel, followed by washing the pad of silica gel with the same solvent (20 mL). The filtrate was washed with water (3 × 15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Preliminary Mechanism Investigation. In two 10 mL Schlenk tubes equipped with a stir bar were placed PhSeCu (0.4 mmol), cyclohexene oxide (1.2 mmol), and K_3PO_4 (1.2 mmol) in DMSO (2 mL). The first tube was evacuated and refilled with N_2 three times. The other tube was fitted with a rubber septum and was then evacuated and refilled with O_2 three times. These reaction mixtures were stirred at 140 °C for 24 h (see Scheme 4, eq 1). To a 10 mL Schlenk tube equipped with a stir bar were placed PhSeCu (0.4 mmol), Se (0.4 mmol), cyclohexene oxide (1.2 mmol), and K_3PO_4 (1.2 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 140 °C for 24 h (see Scheme 4, eq 2). In a 10 mL Schlenk tube equipped with a stir bar were placed iodobenzene (0.4 mmol), cyclohexene oxide (1.2 mmol), Se (0.8 mmol), PhSeCu (10 mol %), and K_3PO_4 (1.2 mmol) in DMSO (2 mL). The tube was evacuated and refilled with N_2 three times. The reaction mixture was stirred at 140 °C for 24 h (see Scheme 4, eq 3). After it was cooled, the reaction mixture was diluted with 10 mL of ethyl ether and filtered through a pad of silica gel, followed by washing the pad of silica gel with the same solvent (20 mL). The filtrate was washed with water (3 × 15 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Characterization Data of Compounds 3 and 4. *2-Phenylselenocyclohexan-1-ol (**3a**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (85.0 mg, 83% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[14]

*2-(2-Cyano)phenylselenocyclohexan-1-ol (**3b**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (64.1 mg, 57% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79−7.77 (m, 1H), 7.70−7.68 (m, 1H), 7.51−7.48 (m, 1H), 7.44−7.41 (m, 1H), 3.48−3.42 (m, 1H), 3.13−3.08 (m, 1H), 2.77 (d, J = 2.5 Hz, 1H), 2.27−2.13 (m, 2H), 1.77−1.65 (m, 2H), 1.44−1.25 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 133.7, 132.7, 131.9, 128.5, 119.5, 118.5, 73.0, 54.8, 34.3, 33.3, 26.8, 24.4. HRMS (ESI): calcd for $C_{13}H_{15}NOSeNa$ $[M + Na]^+$ 304.0212, found 304.0218.

*2-(o-Tolylseleno)cyclohexan-1-ol (**3c**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (87.5 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (d, J = 7.5 Hz, 1H), 7.24−7.18 (m, 2H), 7.09 (t, J = 7.5 Hz, 1H), 3.46−3.41 (m, 1H), 3.00−2.95 (m, 1H), 2.82 (s, 1H), 2.48 (s, 3H), 2.19−2.12 (m, 2H), 1.75−1.19 (m, 1H), 1.50−1.43 (m, 1H), 1.36−1.22 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.5, 135.9, 130.1, 128.9, 128.1, 126.5, 73.1, 53.4, 34.1, 33.4, 26.8, 24.4, 23.3. HRMS (ESI): calcd for $C_{13}H_{18}OSeNa$ $[M + Na]^+$ 293.0416, found 293.0413.

*2-(Naphthalen-1-ylseleno)cyclohexan-1-ol (**3d**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (101.6 mg, 83% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[14]

*2-(3-Fluoro)phenylselenocyclohexan-1-ol (**3e**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (80.0 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36−7.30 (m, 2H), 7.25−7.22 (m, 1H), 7.01 (t, J = 8.5 Hz, 1H), 3.38−3.34 (m, 1H), 2.98−2.93 (m, 1H), 2.80 (s, 1H), 2.20−2.13 (m, 2H), 1.76−1.64 (m, 2H), 1.48−1.20 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.4 (d, J_F = 248.8 Hz), 131.2 (d, J_F = 2.5 Hz), 130.2 (d, J_F = 7.5 Hz), 128.8 (d, J_F = 6.3 Hz), 122.3 (d, J_F = 21.3 Hz), 115.1 (d, J_F = 21.3 Hz), 72.6, 53.9, 34.1, 33.5, 26.8, 24.4. ^{19}F NMR (470 MHz, $CDCl_3$): δ −111.92 (s, 1F). HRMS (ESI): calcd for $C_{12}H_{15}FOSeNa$ $[M + Na]^+$ 297.0165, found 297.0166.

*2-(3-(Trifluoromethyl)phenylseleno)cyclohexan-1-ol (**3f**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (95.9 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, J = 8.0 Hz, 1H), 7.46 (s, 1H), 7.30 (t, J = 8.5 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 3.40−3.34 (m, 1H), 3.00−2.94 (m, 1H), 2.77 (s, 1H), 2.20−2.13 (m, 2H), 1.79−1.74 (m, 1H), 1.68−1.64 (m, 1H), 1.48−1.20 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.1, 133.8, 130.8, 129.1, 127.8, 120.5 (q, J_F = 256.3 Hz), 120.4, 72.7, 53.9, 34.2, 33.47, 26.8, 24.4. ^{19}F NMR (470 MHz, $CDCl_3$): δ −57.81 (s, 3F). HRMS (ESI): calcd for $C_{13}H_{15}F_3OSeNa$ $[M + Na]^+$ 347.0133, found 347.0134.

*2-(3-Nitro)phenylselenocyclohexan-1-ol (**3g**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (78.3 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 3.5−3.40 (m, 1H), 3.09−3.04 (m, 1H), 2.67 (s, 1H), 2.22−2.14 (m, 2H), 1.79−1.67 (m, 2H), 1.50−1.27 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.2, 140.9, 129.9, 129.6, 129.5, 122.7, 72.9, 54.1, 34.4, 33.5, 26.7, 24.3. HRMS (ESI): calcd for $C_{12}H_{16}NO_3Se$ $[M + H]^+$ 302.0290, found 302.0297.

*2-(p-Tolylseleno)cyclohexan-1-ol (**3h**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (92.9 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 3.32−3.27 (m, 1H), 2.97 (s, 1H), 2.85−2.80 (m, 1H), 2.34 (s, 3H), 2.17−2.11 (m, 2H), 1.73−1.70 (m, 1H), 1.63−1.59 (m, 1H), 1.40−1.18 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 136.5, 129.8, 122.6, 72.2, 58.5, 33.9, 33.3, 26.9, 24.5, 21.2. HRMS (ESI): calcd for $C_{13}H_{18}OSeNa$ $[M + Na]^+$ 293.0416, found 293.0418.

*2-(p-Methoxy)phenylselenocyclohexan-1-ol (**3i**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (92.7 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, J = 9.0 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 3.81 (s, 3H), 3.27−3.23 (m, 1H), 2.98 (s, 1H), 2.79−2.73 (m, 1H), 2.13−2.10 (m, 2H), 1.72−1.59 (m, 2H), 1.33−1.19 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9, 138.4, 115.9, 114.7, 71.9, 55.3, 53.4, 33.8, 33.2, 26.9, 24.5. HRMS (ESI): calcd for $C_{13}H_{18}O_2SeNa$ $[M + Na]^+$ 309.0365, found 309.0362.

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*2-(p-Fluoro)phenylselenocyclohexan-1-ol (**3j**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (87.7 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (t, J = 6.5 Hz, 2H), 6.99 (t, J = 8.5 Hz, 2H), 3.29 (s, 1H), 2.87−2.81 (m, 2H), 2.17−2.12 (m, 2H), 1.75−1.72 (m,1H), 1.63−1.62 (m, 1H), 1.38−1.19 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.1 (d, J_F = 247.5 Hz), 138.5 (d, J_F = 8.8 Hz), 120.9, 116.3 (d, J_F = 21.3 Hz), 72.1, 53.7, 33.9, 33.3, 26.8, 24.5. ^{19}F NMR (470 MHz, $CDCl_3$): δ −113.07 (s, 1F). HRMS (ESI): calcd for $C_{12}H_{16}FOSe$ $[M + H]^+$ 275.0345, found 275.0347.

*2-((4-Chlorophenyl)seleno)cyclohexan-1-ol (**3k**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (91.6 mg, 79% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.51 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 3.34−3.29 (m, 1H), 2.91−2.87 (m, 1H), 2.84 (s, 1H), 2.17−2.12 (m, 2H), 1.74−1.62 (m, 2H), 1.43−1.22 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 137.4, 134.6, 129.2, 124.9, 72.3, 53.8, 34.0, 33.7, 26.8, 24.4. HRMS (ESI): calcd for $C_{12}H_{15}ClOSeNa$ $[M + Na]^+$ 312.9870, found 312.9873.

*2-((4-Bromophenyl)seleno)cyclohexan-1-ol (**3l**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (113.6 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46−7.39 (m, 4H), 3.32 (s, 1H), 2.92−2.83 (m, 2H), 2.17−2.12 (m, 2H), 1.75−1.62 (m, 2H), 1.40−1.23 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6, 132.2, 125.6, 122.8, 72.3, 53.8, 34.0, 33.4, 26.8, 24.4. HRMS (ESI): calcd for $C_{12}H_{15}BrOSeNa$ $[M + Na]^+$ 356.9364, found 356.9368.

*2-((4-Formylphenyl)seleno)cyclohexan-1-ol (**3m**).* Following the general procedure, using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (43.2 mg, 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.97 (s, 1H), 7.77−7.70 (m, 4H), 3.47−3.44 (m, 1H), 3.17−3.11 (m, 1H), 2.68 (s, 1H), 2.25−2.15 (m, 2H), 1.79−1.67 (m, 2H), 1.57−1.27 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.6, 137.9, 135.2, 133.9, 129.9, 73.1, 53.7, 34.3, 33.6, 26.8, 24.4. HRMS (ESI): calcd for $C_{13}H_{16}O_2SeNa$ $[M + Na]^+$ 307.0209, found 307.0211.

*2-(p-Methoxycarbonyl)phenylselenocyclohexan-1-ol (**3n**).* Following the general procedure, using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (44.0 mg, 35% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 3.91 (s, 3H), 3.43−3.38 (m, 1H), 3.08−3.03 (m, 1H), 2.75 (s, 1H), 2.22−2.13 (m, 2H), 1.77−1.66 (m, 2H), 1.49−1.26 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.7, 134.7, 134.3, 129.9, 129.3, 72.8, 53.7, 52.22, 34.2, 33.5, 26.8, 24.4. HRMS (ESI): calcd for $C_{14}H_{18}O_3SeNa$ $[M + Na]^+$ 337.0314, found 337.0316.

*2-((3-Chloro-4-amino)phenylseleno)cyclohexan-1-ol (**3o**).* Following the general procedure, using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (95.2 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24−7.21 (m, 1H), 7.16 (d, J = 8.5 Hz, 1H), 6.69 (t, J = 8.5 Hz, 1H), 3.85 (s, 2H), 3.27−3.22 (m, 1H), 2.95 (s, 1H), 2.77−2.71 (m, 1H), 2.13−2.11 (m, 2H), 1.73−1.70 (m, 1H), 1.62−1.60 (m, 1H), 1.36−1.17 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.7, 149.8, 135.3, 133.7, 123.9, 116.9, 71.8, 53.5, 33.8, 33.1, 26.8, 24.5. HRMS (ESI): calcd for $C_{12}H_{16}ClNOSeNa$ $[M + Na]^+$ 327.9979, found 327.9980.

*2-(Thiophen-3-ylseleno)cyclohexan-1-ol (**3p**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (73.4 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44−7.42 (m, 1H), 7.32−7.30 (m, 1H), 7.12 (d, J = 5.0 Hz, 1H), 3.29−3.25 (m, 1H), 2.92 (s, 1H), 2.79−2.74 (m, 1H), 2.18−2.10 (m, 2H), 1.74−1.63 (m, 2H), 1.40−1.18 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.3, 131.1, 126.3, 118.9, 72.2, 53.4, 33.9, 33.3, 26.9, 24.5. HRMS (ESI): calcd for $C_{10}H_{15}OSSe$ $[M + H]^+$ 263.0004, found 263.0008.

*2-(o-Pyridylseleno)cyclohexan-1-ol (**3q**).* Following the general procedure, using 2:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (77.1 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39−8.37 (m, 1H), 7.50−7.44 (m, 2H), 7.09−7.06 (m, 1H), 6.24 (s, 1H), 3.66−3.61 (m, 1H), 3.49−3.43 (m, 1H), 2.28−2.21 (m, 2H), 1.80−1.73 (m, 1H), 1.71−1.70 (m, 1H), 1.61−1.53 (m, 1H), 1.42−1.27 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0, 149.4, 136.5, 126.6, 120.8, 76.1, 50.9, 36.7, 32.6, 26.9, 24.3. HRMS (ESI): calcd for $C_{11}H_{15}NOSeNa$ $[M + Na]^+$ 280.0212, found 280.0211.

*2-(Phenylseleno)cyclopentan-1-ol (**4a**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (92.0 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58−7.55 (m, 2H), 7.28−7.26 (m, 3H), 4.18−4.15 (m, 1H), 3.42−3.38 (m, 1H), 2.30−2.23 (m, 1H), 2.09−2.03 (m, 1H), 1.82−1.60 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.20, 129.36, 129.11, 127.48, 79.06, 49.29, 32.90, 31.12, 22.05. HRMS (ESI): calcd for $C_{11}H_{14}OSeNa$ $[M + Na]^+$ 265.0103, found 265.0101.

*4-((2-Hydroxycyclohexyl)seleno)tetrahydrofuran-3-ol (**4b**).* Following the general procedure, using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (79.1 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57−7.54 (m, 2H), 7.30−7.27 (m, 3H), 4.37−4.31 (m, 2H), 4.02 (dd, J_1 = 4.5 Hz, J_2 = 9.5 Hz, 1H), 3.77−3.72 (m, 2H), 3.63−3.60 (m, 1H), 2.63 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.1, 129.4, 128.7, 127.9, 77.8, 74.0, 72.2, 47.4. HRMS (ESI): calcd for $C_{10}H_{12}O_2SeNa$ $[M + Na]^+$ 266.9896, found 266.9898.

*2-Methyl-1-(phenylseleno)propan-2-ol (**4c**).* Following the general procedure, using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (59.8 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56−7.54 (m, 2H), 7.26−7.23 (m, 3H), 3.15 (s, 2H), 2.26 (s, 1H), 1.31 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 132.5, 130.9, 129.2, 127.0, 70.4, 44.4, 29.0. HRMS (ESI): calcd for $C_{10}H_{14}OSeNa$ $[M + Na]^+$ 253.0103, found 253.0106.

*1-(Phenylseleno)butan-2-ol (**4d**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (85.6 mg, 93% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[16]

*3,3-Dimethyl-1-(phenylseleno)butan-2-ol (**4e**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (82.6 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52−7.50 (m, 2H), 7.27−7.25 (m, 3H), 3.27 (dd, J_1 = 11.0 Hz, J_2 = 26.0 Hz, 2H), 2.80 (t, J = 12.0 Hz, 1H), 2.49 (s, 1H), 0.92 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 132.9, 129.4, 129.2, 127.2, 77.1, 34.9, 33.3, 25.8. HRMS (ESI): calcd for $C_{12}H_{18}OSeNa$ $[M + Na]^+$ 281.0416, found 281.0417.

*1-Butoxyl-3-(phenylseleno)-propan-2-ol (**4f**).* Following the general procedure, after 12 h butyl glycidyl ether (156 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (99.1 mg, 86% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[17]

*4-(Phenylseleno)buten-3-ol (**4g**).* Following the general procedure, using 8:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (52.9 mg, 58% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[18]

*1-(Phenylseleno)-3-(2-propen-1-yloxy)-propan-2-ol (**4h**).* Following the general procedure, after 12 h allyl glycidyl ether (136.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (77.2 mg, 71% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[17]

*2′-Propenoic Acid-2-hydroxy-3-(phenylseleno)propyl Ester (**4i**).* Following the general procedure, after 12 h glycidyl methacrylate (170.4 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (36 mg, 30% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[17]

*1-Phenoxy-3-(phenylseleno)propan-2-ol (**4j**).* Following the general procedure, after 12 h glycidyl phenyl ether (180.0 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (82.6 mg, 67% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[17]

*1-(p-Fluoro)phenoxy-3-(phenylseleno)propan-2-ol (**4k**).* Following the general procedure, after 12 h (4-fluoro)phenoxymethyl oxirane (201.6 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using

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4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (122.6 mg, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55−7.53 (m, 2H), 7.25−7.23 (m, 3H), 6.96−6.92 (m, 2H), 6.80−6.77 (m, 2H), 4.11−4.07 (m, 1H), 4.01−3.95 (m, 2H), 3.22−3.19 (m, 1H), 3.14−3.10 (m, 1H), 2.68 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5 (d, J_F = 237.5 Hz), 154.5 (d, J_F = 1.3 Hz), 132.9, 129.3, 129.2, 127.4, 115.9 (d, J_F = 23.8 Hz), 115.6 (d, J_F = 8.8 Hz), 71.2, 69.0, 31.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ −123.35 (s, 1F). HRMS (ESI): calcd for $C_{15}H_{15}FO_2SeNa$ $[M + Na]^+$ 349.0114, found 349.0120.

*1-(p-Chloro)phenoxy-3-(phenylseleno)propan-2-ol (**4l**).* Following the general procedure, after 12 h (4-chloro)phenoxymethyl oxirane (220.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (101.2 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.52 (m, 2H), 7.25−7.24 (m, 3H), 7.20 (d, J = 9.0 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 4.12−4.07 (m, 1H), 4.01−3.95 (m, 2H), 3.20 (dd, J_1 = 5.5 Hz, J_2 = 13.0 Hz, 1H), 3.12 (dd, J_1 = 7.0 Hz, J_2 = 13.0 Hz, 1H), 2.73 (d, J = 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.0, 133.0, 129.4, 129.3, 129.1, 127.5, 126.1, 115.8, 70.8, 69.0, 31.9. HRMS (ESI): calcd for $C_{15}H_{15}ClO_2SeNa$ $[M + Na]^+$ 364.9819, found 364.9814.

*1-(p-Bromo)phenoxy-3-(phenylseleno)propan-2-ol (**4m**).* Following the general procedure, after 12 h (4-bromo)phenoxymethyl oxirane (273.6 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (118.9 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.52 (m, 2H), 7.36−7.33 (m, 2H), 7.25−7.24 (m, 3H), 6.74−6.71 (m, 2H), 4.11−4.07 (m, 1H), 4.00−3.95 (m, 2H), 3.20 (dd, J_1 = 6.0 Hz, J_2 = 13.0 Hz, 1H), 3.11 (dd, J_1 = 7.0 Hz, J_2 = 13.0 Hz, 1H), 2.67 (d, J = 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.5, 133.0, 132.3, 129.3, 129.1, 127.5, 116.4, 113.4, 70.8, 68.9, 31.9. HRMS (ESI): calcd for $C_{15}H_{15}BrO_2SeNa$ $[M + Na]^+$ 408.9314, found 408.9310.

*1-(p-Methoxyl)phenoxy-3-(phenylseleno)propan-2-ol (**4n**).* Following the general procedure, after 12 h (4-methoxy)phenoxymethyl oxirane (216.0 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (117.6 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.52 (m, 2H), 7.24−7.23 (m, 3H), 6.81−6.75 (m, 4H), 4.10−4.07 (m, 1H), 4.00−3.93 (m, 2H), 3.75 (s, 3H), 3.20 (dd, J_1 = 6.0 Hz, J_2 = 13.0 Hz, 1H), 3.11 (dd, J_1 = 7.0 Hz, J_2 = 13.0 Hz, 1H), 2.81 (d, J = 4.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.2, 152.5, 132.9, 129.4, 129.3, 127.4, 115.6, 114.7, 71.3, 69.2, 55.8, 31.9. HRMS (ESI): calcd for $C_{16}H_{18}O_3SeNa$ $[M + Na]^+$ 361.0314, found 361.0318.

*1-(p-Trifluoromethyl)phenoxy-3-(phenylseleno)propan-2-ol (**4o**).* Following the general procedure, after 12 h (4-trifluoromethyl)-phenoxymethyl oxirane (261.6 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (93.3 mg, 62% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.50 (m, 4H), 7.24−7.23 (m, 3H), 6.89 (d, J = 8.55 Hz, 2H), 4.14−4.11 (m, 1H), 4.07−4.01 (m, 2H), 3.22 (dd, J_1 = 5.5 Hz, J_2 = 13.0 Hz, 1H), 3.13 (dd, J_1 = 7.0 Hz, J_2 = 13.0 Hz, 1H), 2.78 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.8, 133.1, 129.3, 128.9, 127.6, 127.0, 126.9, 126.8, 125.4, 123.4 (q, J_F = 31.3 Hz), 114.5, 70.6, 68.9, 31.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ −61.55 (s, 3F). HRMS (ESI): calcd for $C_{16}H_{15}F_3O_2SeNa$ $[M + Na]^+$ 399.0082, found 399.0084.

*1-Phenyl-2-(phenylseleno)ethan-1-ol (**4p**).* Following the general procedure, after 12 h phenyl oxirane (144 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (84.5 mg, 76% yield). The ^{1}H and ^{13}C NMR spectra were in accordance with those described in the literature.[18]

*1-(4-Fluoro)phenyl-2-phenylselenoethan-1-ol (**4q**).* Following the general procedure, after 12 h (4-fluoro)phenyl oxirane (184.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (92.4 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55−7.52 (m, 2H), 7.31−7.27 (m, 5H), 7.01 (t, J = 8.5 Hz, 2H), 4.72−4.70 (m, 1H), 3.26 (dd, J_1 = 3.5 Hz, J_2 = 13.0 Hz, 1H), 3.09 (dd, J_1 = 9.5 Hz, J_2 = 13.0 Hz, 1H), 2.85 (s,1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.4 (d, J_F = 248.7 Hz), 138.2 (d, J_F = 3.7 Hz), 133.2, 129.3, 128.9, 127.5, 127.5, 115.4 (d, J_F = 21.2 Hz), 71.6, 38.6. ^{19}F NMR (470 MHz, $CDCl_3$): δ −114.40 (s, 1F). HRMS (ESI): calcd for $C_{14}H_{14}FOSe$ $[M + H]^+$ 297.0189, found 297.0183.

*1-(4-Chloro)phenyl-2-phenylselenoethan-1-ol (**4r**).* Following the general procedure, after 12 h (4-chloro)phenyl oxirane (184.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (93.6 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52−7.50 (m, 2H), 7.28−7.23 (m, 7H), 4.68 (d, J = 9.0 Hz, 1H), 3.24 (dd, J_1 = 3.5 Hz, J_2 = 13.0 Hz, 1H), 3.05 (dd, J_1 = 9.0 Hz, J_2 = 13.0 Hz, 1H), 2.93 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.9, 133.6, 133.3, 129.4, 128.9, 128.7, 127.6, 127.3, 71.5, 38.4. HRMS (ESI): calcd for $C_{14}H_{14}ClOSe$ $[M + H]^+$ 312.9893, found 312.9891.

*1-(4-Bromo)phenyl-2-phenylselenoethan-1-ol (**4s**).* Following the general procedure, after 12 h (4-bromo)phenyl oxirane (237.6 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (102.5 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.50 (m, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.29−7.27 (m, 3H), 7.19 (d, J = 8.5 Hz, 2H), 4.69−4.66 (m, 1H), 3.25 (dd, J_1 = 3.5 Hz, J_2 = 12.5 Hz, 1H), 3.06 (dd, J_1 = 9.0 Hz, J_2 = 12.5 Hz, 1H), 2.87 (d, J = 3.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.5, 133.3, 131.6, 129.4, 128.8, 127.6, 127.6, 121.7, 71.6, 38.4. HRMS (ESI): calcd for $C_{14}H_{14}BrOSe$ $[M + H]^+$ 356.9388, found 356.9390.

*1-(2-Chloro)phenyl-2-phenylselenoethan-1-ol (**4t**).* Following the general procedure, after 12 h (2-chloro)phenyl oxirane (184.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (84.9 mg, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64−7.56 (m, 3H), 7.29−7.17 (m, 6H), 5.12−5.09 (m, 1H), 3.47 (dd, J_1 = 2.5 Hz, J_2 = 13.0 Hz, 1H), 2.95 (dd, J_1 = 9.5 Hz, J_2 = 13.0 Hz, 1H), 2.92 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.8, 133.2, 131.7, 129.4, 129.2, 128.8, 128.7, 127.5, 127.2, 127.01, 68.7, 36.6. HRMS (ESI): calcd for $C_{14}H_{14}ClOSe$ $[M + H]^+$ 312.9893, found 312.9890.

*1-(Phenylmethoxy)-3-(phenylseleno)-propan-2-ol (**4u**).* Following the general procedure, after 12 h benzyl glycidyl ether (196.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (109.5 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52−7.50 (m, 2H), 7.35−7.30 (m, 2H), 7.30−7.28 (m, 3H), 7.24−7.23 (m, 3H), 4.49 (s, 2H), 3.94−3.90 (m, 1H), 3.56 (dd, J_1 = 4.0 Hz, J_2 = 9.5 Hz, 1H), 3.51 (dd, J_1 = 6.0 Hz, J_2 = 9.5 Hz, 1H), 3.08 (dd, J_1 = 5.5 Hz, J_2 = 12.5 Hz, 1H), 3.02 (dd, J_1 = 7.0 Hz, J_2 = 12.5 Hz, 1H), 2.72 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.8, 132.9, 129.6, 129.2, 128.5, 127.9, 127.8, 127.2, 73.4, 72.9, 69.5, 31.9. HRMS (ESI): calcd for $C_{16}H_{18}O_2SeNa$ $[M + Na]^+$ 345.0365, found 345.0369.

*1-(Furan-2-ylmethoxy)-3-(phenylselanyl)propan-2-ol (**4v**).* Following the general procedure, after 12 h furfuryl glycidyl ether (184.8 mg, 3 equiv, 1.2 mmol) was added using a syringe, and using 4:1 petroleum ether/ethyl acetate as the eluant afforded a yellow oily liquid (76.1 mg, 61% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52−7.50 (m, 2H), 7.39 (s, 1H), 7.26−7.24 (m, 3H), 6.34−6.33 (m, 1H), 6.30−6.29 (m, 1H), 4.44 (s, 2H), 3.91−3.86 (m, 1H), 3.56 (dd, J_1 = 4.0 Hz, J_2 = 9.5 Hz, 1H), 3.48 (dd, J_1 = 6.0 Hz, J_2 = 9.5 Hz, 1H), 3.06 (dd, J_1 = 5.5 Hz, J_2 = 12.5 Hz, 1H), 2.99 (dd, J_1 = 7.0 Hz, J_2 = 12.5 Hz, 1H), 2.61 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.4, 142.9, 132.8, 129.6, 129.2, 127.2, 110.3, 109.5, 72.7, 69.4, 65.4, 31.9. HRMS (ESI): calcd for $C_{14}H_{16}O_3SeNa$ $[M + Na]^+$ 335.0158, found 335.0155.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01274.

^{1}H, ^{13}C and ^{19}F NMR spectral data of all compounds reported (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) For selected reviews, see: (a) Mugesh, G.; du Mont, W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125. (b) Mugesh, G.; Singh, H. B. *Acc. Chem. Res.* **2002**, *35*, 226. (c) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, *104*, 6255. (d) Manjare, S. T.; Kim, Y.; Churchill, D. G. *Acc. Chem. Res.* **2014**, *47*, 2985.

(2) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697.

(3) (a) Rémion, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1976**, *17*, 1385. (b) Piers, E.; Nagakura, I. *Tetrahedron Lett.* **1976**, *17*, 3237.

(4) (a) Van Ende, D.; Dumont, W.; Hevesi, L.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 700. (b) Dumont, W.; Krief, A. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 350. (c) Van Ende, D.; Krief, A. *Tetrahedron Lett.* **1976**, *17*, 457.

(5) Zanella, R.; Ros, R.; Grazian, M. *Inorg. Chem.* **1973**, *12*, 2736.

(6) Taniguchi, N. *Synlett* **2005**, *11*, 1687.

(7) (a) Singh, D.; Deobald, A. M.; Camargo, L. R. S.; Tabarelli, G.; Rodrigues, O. E. D.; Braga, A. L. *Org. Lett.* **2010**, *12*, 3288. (b) Li, Y.; Nie, C.; Wang, H.; Li, X.; Verpoort, F.; Duan, C. *Eur. J. Org. Chem.* **2011**, *2011*, 7331. (c) Taniguchi, N. *Tetrahedron* **2012**, *68*, 10510. (d) Li, Z.; Ke, F.; Deng, H.; Xu, H.; Xiang, H.; Zhou, X. *Org. Biomol. Chem.* **2013**, *11*, 2943. (e) Shibahara, F.; Kanai, T.; Yamaguchi, E.; Kamei, A.; Yamauchi, T.; Murai, T. *Chem. - Asian J.* **2014**, *9*, 237.

(8) Balkrishna, S. J.; Bhakuni, B. S.; Chopra, D.; Kumar, S. *Org. Lett.* **2010**, *12*, 5394.

(9) (a) Wu, B.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 10496. (b) Fang, Y.; Wang, S. Y.; Shen, X.-B.; Ji, S.-J. *Org. Chem. Front.* **2015**, *2*, 1338.

(10) (a) Chen, C.; Hou, C.; Wang, Y.; Hor, T. S.; Weng, Z. *Org. Lett.* **2014**, *16*, 524. (b) Lefebvre, Q.; Pluta, R.; Rueping, M. *Chem. Commun.* **2015**, *51*, 4394.

(11) Luo, D.; Wu, G.; Yang, H.; Liu, M.; Gao, W.; Huang, X.; Chen, J.; Wu, H. *J. Org. Chem.* **2016**, *81*, 4485.

(12) (a) Azuma, H.; Tamagaki, S.; Ogino, K. *J. Org. Chem.* **2000**, *65*, 3538. (b) Rigby, J. H.; Maharoof, U. S. M.; Mateo, M. E. *J. Am. Chem. Soc.* **2000**, *122*, 6624. (c) Treadwell, E. M.; Neighbors, J. D.; Wiemer, D. F. *Org. Lett.* **2002**, *4*, 3639. (d) Bagul, T. D.; Lakshmaiah, G.; Kawabata, T.; Fuji, K. *Org. Lett.* **2002**, *4*, 249. (e) Knapp, S.; Zhao, D. L. *Org. Lett.* **2000**, *2*, 4037.

(13) (a) Liotta, D.; Sunay, U.; Santiesteban, H.; Markiewicz, W. *J. Org. Chem.* **1981**, *46*, 2605. (b) Nishiyama, Y.; Ohashi, H.; Itoh, K.; Sonoda, N. *Chem. Lett.* **1998**, 159. (c) Dowsland, J.; McKerlie, F.; Procter, D. J. *Tetrahedron Lett.* **2000**, *41*, 4923. (d) Sridhar, R.; Srinivas, B.; Surendra, K.; Krishnaveni, N. S.; Rao, K. R. *Tetrahedron Lett.* **2005**, *46*, 8837. (e) Santi, C.; Santoro, S.; Battistelli, B.; Testaferri, L.; Tiecco, M. *Eur. J. Org. Chem.* **2008**, *2008*, 5387. (f) Freudendahl, D. M.; Shahzad, S. A.; Wirth, T. *Eur. J. Org. Chem.* **2009**, *2009*, 1649. (g) Lv, G.; Li, T.; Hu, R.; Chen, J.; Ding, J.; Wu, H. J. *J. Chem. Res.* **2010**, *34*, 549.

(14) Lu, X. Y.; Yang, C. T.; Liu, J. H.; Zhang, Z. Q.; Lu, X.; Xiao, B.; Fu, Y. *Chem. Commun.* **2015**, *51*, 2388.

(15) Yang, M. H.; Yan, G. B.; Zheng, Y. F. *Tetrahedron Lett.* **2008**, *49*, 6471.

(16) Sheng, S. R.; Luo, H. R.; Huang, Z. Z.; Sun, W. K.; Liu, X. L. *Synth. Commun.* **2007**, *37*, 2693.

(17) Lv, G. S.; Li, T.; Hu, R. J.; Chen, J. X.; Ding, J. C.; Wu, H. Y. *J. Chem. Res.* **2010**, *34*, 549.

(18) Gruttadauria, M.; Meo, P.; Riela, S.; D'Anna, F.; Noto, R. *Tetrahedron: Asymmetry* **2006**, *17*, 2713.

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