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Abstract:

Organoselenium compounds have attracted sustained interest because of their distinctive chemical reactivity and broad biological relevance. Selenium-mediated functionalization of carbonyls provides direct access to valuable selenium-containing building blocks. Herein, we report a simple electrochemical flow protocol for the α -selenylation of β -ketoesters using readily available diselenides. The reaction was developed in a commercially available undivided electrochemical flow cell using graphite electrodes and lithium perchlorate as supporting electrolyte. Systematic investigation of current, charge, flow rate, diselenide stoichiometry, and substrate concentration identified optimal conditions with a residence time of 4 min. Under these conditions, a range of para and meta-substituted β -ketoesters underwent efficient α -selenylation, providing the corresponding α -seleno derivatives in 60–85% yield. The method provides rapid access to synthetically useful α -selenylated building blocks and highlights the potential of electrochemical flow technology for the preparation and subsequent telescoped synthesis of selenium-containing heterocycles.

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Electrochemical Flow α -Selenylation of 1,3-Dicarbonyl Compounds with Diselenides

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Abstract Organoselenium compounds have attracted sustained interest because of their distinctive chemical reactivity and broad biological relevance. Selenium-mediated functionalization of carbonyls provides direct access to valuable selenium-containing building blocks. Herein, we report a simple electrochemical flow protocol for the α -selenylation of β -ketoesters using readily available diselenides. The reaction was developed in a commercially available undivided electrochemical flow cell using graphite electrodes and lithium perchlorate as supporting electrolyte. Systematic investigation of current, charge, flow rate, diselenide stoichiometry, and substrate concentration identified optimal conditions with a residence time of 4 min. Under these conditions, a range of *para*- and *meta*-substituted β -ketoesters underwent efficient α -selenylation, providing the corresponding α -seleno derivatives in 60–85% yield. The method provides rapid access to synthetically useful α -selenylated building blocks and highlights the potential of electrochemical flow technology for the preparation and subsequent telescoped synthesis of selenium-containing heterocycles.

Key words organoselenium chemistry; electrochemical synthesis; flow chemistry; α -selenylation; β -ketoesters; diselenides; cyclic voltammetry

Organoselenium chemistry became a recognized tool in the 1970s following the discovery that selenation of enolates provides α -selenocarbonyl compounds that can undergo oxidative elimination to furnish α,β -unsaturated carbonyl compounds.^{2–6}

Selenium is an essential trace element in biological systems, occurring naturally in compounds such as selenocysteine. Incorporation of selenium into organic molecules can significantly alter their physicochemical and biological properties. In medicinal chemistry, selenium has frequently been considered as a bioisosteric replacement for sulfur or oxygen, while selenium-containing compounds can exhibit antioxidant,

antimicrobial, anti-inflammatory, and other biologically relevant properties.^{7–12}

Beyond their biological importance, organoselenium compounds possess attractive synthetic properties. Selenium-containing groups can be introduced into organic molecules under mild reaction conditions and subsequently transformed or removed selectively. Selenium-mediated transformations have therefore found applications in functional-group manipulation, catalysis, and the synthesis of structurally complex molecules.^{7,13–16}

1,3-Dicarbonyl compounds are particularly attractive synthetic substrates because of their accessibility, tuneable reactivity, and extensive application as precursors to biologically active molecules and heterocyclic systems.^{17,18} α -Selenylated 1,3-dicarbonyl compounds are consequently useful intermediates that can participate in subsequent transformations leading to structurally diverse selenium-containing molecules.

Known methods for the preparation of α -selenylated 1,3-dicarbonyl compounds are relatively limited and have traditionally relied on the electrophilic selenylation of preformed enolates or enol derivatives using reagents such as phenylselenyl halides and *N*-(phenylseleno)phthalimide.^{19,20,21} Classical approaches also include the use of selenium-stabilised organolithium intermediates and related selenoacetals, although these methods generally require prefunctionalization and strong bases. More recently, oxidative C–Se bond formation including K₂S₂O₈-mediated protocols have provided a direct alternative.²²

Electrochemical synthesis offers an attractive approach to such transformations because electrons can serve as traceless redox reagents, potentially avoiding the need for stoichiometric chemical oxidants or reductants.²³ Furthermore, continuous-flow electrochemistry provides efficient mass and heat transfer and allows precise control of residence time and charge delivery. These characteristics can be particularly advantageous for reactions in which overoxidation of the desired product is a competing process.^{24–27}

Herin, we describe the direct α -selenylation of β -ketoesters using organic diselenides under electrochemical flow conditions. The study focused on identifying suitable electrolysis parameters, establishing the substrate scope, and gaining mechanistic insight through cyclic voltammetry.

Ethyl 3-oxo-3-phenylpropanoate **1a** and diphenyl diselenide **2** were selected as substrates for the development of the reaction, producing ethyl 3-oxo-3-phenyl-2-(phenylselenanyl)propanoate **3a**. Initial experiments were performed with a commercial Ion electrochemical flow cell equipped and an undivided reactor configuration. In previous experiments we already had established that graphite electrodes are optimal for selenylation reactions.²⁵

At a flow rate of 0.10 mL min⁻¹ and a substrate concentration of 0.05 M, variation of the applied current between 16 and 32 mA demonstrated a clear dependence of the reaction outcome on the amount of charge passed (Table 1). The desired α -selenylated product was obtained under all conditions examined.

Table 1 Electrochemical α -selenylation of β -ketoester **1a** using diphenyl diselenide **2**: current, charge and flow rate screening.^a

Entry	Current (mA)	Charge (F)	% Yield 3a ^b
1	16	2.0	53
2	18	2.25	55
3	20	2.5	62
4	22	2.75	52
5	24	3.0	67
6	28	3.5	60
7	32	4.0	24
8 ^c	30	2.5	73
9 ^c	36	3.0	55

^a graphite electrodes, FEP (fluorinated ethylene propylene) spacer (500 μ m thickness; reactor volume: 0.6 mL; electrode area: 12 cm²); [**1a**] = 0.05 M; [**2a**] = 0.06 M; [LiClO₄] = 0.04 M; solvent: acetonitrile; flow rate = 0.1 mL min⁻¹; calculated residence time = 6.0 min. ^b Determined by ¹H NMR with 1,3,5-trimethoxybenzene as internal standard. ^c flow rate = 0.15 mL min⁻¹.

At 16 mA, corresponding to 2.0 F mol⁻¹ under the stated conditions, **3a** was obtained in 53% yield (Table 1, entry 1). Highest yields of **3a** (67%) were obtained after further increase to 24 mA (3.0 F mol⁻¹; Table 1, entries 2–5), whereas at 32 mA, corresponding to 4.0 F mol⁻¹, the yield decreased dramatically to 24% (Table 1, entry 7). These observations indicate that increasing the charge does not continuously improve conversion to the desired product. In particular, the pronounced decrease at 4.0 F mol⁻¹ is consistent with further electrochemical oxidation or degradation of the α -selenylated product **3a**. The degradation products could not be identified.

The influence of flow rate was subsequently examined because residence time represents a critical parameter in continuous electrochemical synthesis. Experiments were performed at 2.5 and 3.0 F mol⁻¹ while varying the flow rate. Increasing the flow rate to 0.15 mL min⁻¹ while maintaining 2.5 F mol⁻¹ increased the yield to 73% of **3a**, corresponding to a calculated residence time

of 4 min (Table 1, entry 8). Increasing the charge to 3.0 F mol⁻¹ at this flow rate again resulted in a reduction in yield, giving **3a** in 55% (Table 1, entry 9).

These results demonstrate that the balance between electrochemical charge and residence time is crucial. Shorter residence times can reduce exposure of the newly formed α -selenylated product to the electrode environment and thereby minimise secondary oxidation or decomposition. The optimal combination identified was therefore a flow rate of 0.15 mL min⁻¹ and 2.5 F mol⁻¹, providing **3a** in 73% yield.

The amount of diphenyl diselenide **2** was subsequently varied between 1.0 and 1.5 equivalents. Using one equivalent of diselenide resulted in 60% yield of **3a**, while increasing the amount to 1.15 equivalents improved the yield to 66%. The highest yield, 73%, was obtained using 1.33 equivalents. Further increasing the diselenide loading to 1.5 equivalents did not provide additional benefit and resulted in a slightly reduced yield of 67%. Accordingly, 1.33 equivalents were selected for subsequent experiments.

Finally, the concentration of the β -ketoester was examined. A concentration of 0.05 M gave the highest yield of 73%. Dilution to 0.04 M resulted in a substantial decrease in yield to 45%. Increasing the concentration to 0.075 and 0.10 M gave 60% and 57% yields, respectively. Although the more concentrated reactions provided lower isolated conversion to the desired product, they may nevertheless offer advantages in terms of productivity and warrant further investigation for scale-up applications.

With the established optimised reaction conditions, the generality of the transformation was investigated using a variety of substituted β -ketoesters. The reaction demonstrated good tolerance towards electron-withdrawing and electron-donating substituents on the aromatic ring.

The parent substrate afforded α -selenylated product **3a** in 85% yield. *Para*-substituted substrates containing CF₃ and F groups gave the corresponding products **3b** and **3c** in 67% and 62% yield, respectively. The *para*-bromo and *para*-chloro derivatives provided the products **3d** and **3e** in 64% and 70% yield, respectively. Notably, the electron-rich *para*-methoxy substrate underwent successful α -selenylation to **3f** in 76% yield despite the potential susceptibility of the methoxy-substituted aromatic ring to oxidation.

Alkyl-substituted substrates also participated in the reaction, with *para*-*tert*.-butyl-, *para*-methyl- and *para*-phenyl-substituted β -ketoesters furnishing the corresponding products **3g**, **3h** and **3i** in around 60% yield in each case.

The method was similarly effective with *meta*-substituted substrates. Fluoro-, bromo-, and methoxy-containing β -ketoesters gave the corresponding α -selenylated products **3j**–**3l** in 71%, 66%, and 79% yield, respectively. Overall, the transformation tolerated a diverse range of electronic properties and substituent types, with product yields ranging from 60 to 85%.²⁹

Importantly, the flow electrochemical protocol generally provided slightly higher yields than the corresponding batch electrochemical reactions examined for the substrate series. The yields of the batch reactions are also indicated in Table 2. These

results demonstrate the potential advantage of continuous processing for this transformation, particularly where control of residence time and avoidance of prolonged electrochemical exposure are important.

In addition, a scale-up electrolysis was performed using 8.1 mmol of **1a**. This was converted into 1.7 g **3a** (60%) within 18 hours using the flow reaction conditions described above, resulting in a productivity of 94 mg h⁻¹ for a single reactor. Upscaling through multiple parallel reactors could be achieved easily, as we have demonstrated recently in different electrochemical reactions.³⁰

Table 2 Substrate scope of the electrochemical α -selenylation of β -ketoesters **1**.

Entry	R	% Yield 3 (Batch) ^a	% Yield 3 (Flow) ^b
1	H	3a : 75	3a : 85
2	4-CF ₃	3b : 53	3b : 67
3	4-F	3c : 45	3c : 62
4	4-Br	3d : 55	3d : 64
5	4-Cl	3e : 53	3e : 70
6	4-OMe	3f : 57	3f : 76
7	4- <i>t</i> -Bu	3g : 55	3g : 60
8	4-Me	3h : 45	3h : 60
9	4-Ph	3i : 47	3i : 62
10	3-F	3j : 53	3j : 71
11	3-Br	3k : 44	3k : 66
12	3-OMe	3l : 55	3l : 79

^a Batch electrolysis was performed using the IKA Electrasyn 2.0. A solution of substrate **1** (0.15 mmol, 1 equiv.), diphenyl diselenide **2** (0.4 mmol, 2.6 equiv.) and acetonitrile (5 mL) was electrolysed using an undivided cell (5 mL glass vial) with graphite electrodes, under constant current of 7 mA with stirring (420 rpm) for 90 min (2.5 F). ^b graphite electrodes, FEP spacer (500 μ m thickness; reactor volume: 0.6 mL; electrode area: 12 cm²); [**1a**] = 0.05 M; [**2**] = 0.06 M; [LiClO₄] = 0.04 M; solvent: acetonitrile; flow rate = 0.15 mL min⁻¹; calculated residence time = 4.0 min.

Cyclic voltammetry was employed to obtain further insight into the electrochemical behaviour of the reaction components. Measurements were performed for the β -ketoester **1a**, diphenyl diselenide **2**, and their combination in acetonitrile with Bu₄NBF₄ as supporting electrolyte.

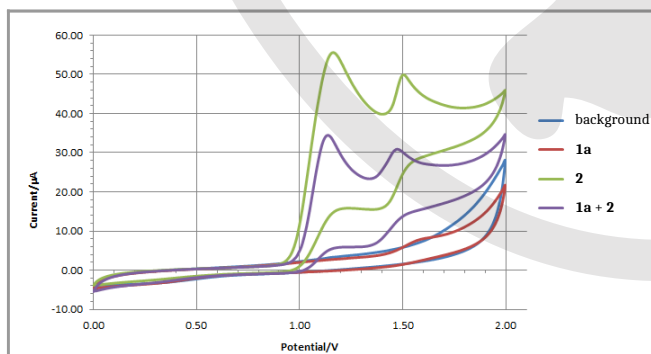


Figure 1 Cyclic voltammograms of reactants and their mixtures in 0.1 M Bu₄NBF₄/MeCN using a glassy carbon disk working electrode, Pt wire counter electrode and Ag/AgNO₃ as

a reference electrode at 100 mV/s scan rate; blue line: Bu₄NBF₄ (0.1 M/MeCN), red line: **1a** (1 mM), green line **2** (1 mM), and purple line **1a** + **2** (1 mM each).

The voltammogram of diphenyl diselenide displayed two oxidation features at approximately 1.18 and 1.52 V (Figure 1). In contrast, the β -ketoester showed no prominent oxidation signal under the same conditions. The mixture displayed electrochemical behaviour consistent with preferential oxidation of diphenyl diselenide relative to the β -ketoester.

Based on these observations and precedent in organoselenium electrochemistry, initial oxidation of diphenyl diselenide at the anode generates a radical cation and an electrophilic selenium species. These reactive selenium intermediates can react with the enol form of the β -ketoester, ultimately providing the α -selenylated product. At the cathode, proton reduction provides the complementary reduction process, with hydrogen evolution representing the cathodic reaction. The cyclic voltammetry data therefore support a reaction pathway in which the diselenide, rather than the β -ketoester, undergoes the initial anodic oxidation.

A straightforward electrochemical flow protocol for the α -selenylation of β -ketoesters with organic diselenides has been developed. The transformation uses a commercially available undivided electrochemical flow cell and avoids the requirement for a conventional stoichiometric chemical oxidant. Optimisation demonstrated that the reaction outcome is strongly dependent on the interplay between applied charge and residence time, with the best performance obtained at 30 mA, corresponding to 2.5 F mol⁻¹, and a flow rate of 0.15 mL min⁻¹.

Under these conditions, a range of β -ketoesters bearing electron-withdrawing, electron-donating, and alkyl substituents underwent α -selenylation to furnish the corresponding products in 60–85% yield. The successful transformation of an oxidation-sensitive methoxy-substituted substrate is particularly noteworthy and illustrates the potential benefit of controlling residence time under continuous-flow electrolysis.

Cyclic voltammetry indicated preferential anodic oxidation of the diselenide, supporting a mechanistic proposal involving electrochemical activation of the Se–Se bond followed by reaction with the enol form of the β -ketoester, similar to previously reported mechanisms.^{25,27,28}

The α -selenylated 1,3-dicarbonyl compounds generated by this method represent useful synthetic intermediates for further functionalisation. An important future direction will therefore be the direct telescoping of the electrochemical selenylation with subsequent condensation reactions. In particular, coupling the output of the electrochemical reactor with a second stream containing dinucleophilic reagents such as hydrazine derivatives could enable the continuous synthesis of selenium-containing heterocycles without isolation of the intermediate α -selenylated compounds. Such coupled flow/flow processes could provide a rapid and modular approach to structurally diverse organoselenium compounds in the future.

AI Declaration

GenAI has not been used, to my knowledge, to prepare the manuscript.

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Supporting Information

NO (this text will be deleted prior to publication)

Primary Data

NO.

Conflict of Interest

The authors declare no conflict of interest.

References and Notes

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- (29) General experimental procedures: **(Batch)**: Electrolysis was performed using the IKA Electrasyn 2.0. A solution of substrate **1** (0.15 mmol), diphenyl diselenide **2** (0.4 mmol, 2.6 equiv.) and $LiClO_4$ (0.1 M) in acetonitrile (5 mL) was electrolyzed using an undivided cell (5 mL glass vial) equipped with graphite electrodes under constant current of 7 mA with stirring (420 rpm) for 90 min (2.5 F). After the electrolysis, the solvent was evaporated in vacuo. The crude product was purified by flash chromatography on silica gel (petroleum ether / ethyl acetate 3:2).
(Flow) The electrolysis was performed in an undivided cell using a Vapourtec Ion Electrochemical Flow Reactor (reactor volume 0.6 mL, spacer 0.5 mm), using graphite electrodes (active surface area = 12 cm² for each electrode). A solution of the β -ketoester derivative **1** (1.25 mmol, 0.05 M) was dissolved with diphenyl diselenide **2** (1.66 mmol, 0.06 M, 1.33 equiv.) and $LiClO_4$ (1 mmol, 0.04 M) in acetonitrile (25 mL) and pumped with a flow rate of 0.15 mL min⁻¹ and electrolysed under constant current conditions (30 mA, 2.5 F/mol). After reaching a steady state, the product solution was collected for a defined period and the solvent was removed under vacuum. The crude product was purified by column chromatography (petroleum ether / ethyl acetate 3:2).
Ethyl 3-oxo-3-phenyl-2-(phenylselenanyl)propanoate (3a)
Batch: 39 mg, 0.112 mmol, 75%. Flow: 369 mg, 1.06 mmol, 85%.
¹H NMR (500 MHz, CDCl₃) δ = 7.87 (dd, *J* = 8.5, 1.2 Hz, 2H), 7.60 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.44 – 7.39 (m, 2H), 7.36 – 7.26 (m, 3H), 5.34 (s, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H) ppm.
¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.8, 168.0, 135.9, 135.1, 133.6, 129.2, 129.0, 128.8, 128.6, 127.5, 62.3, 51.5, 13.8 ppm.
HRMS (ES⁺) *m/z*: [M+H]⁺ calcd for C₁₇H₁₇O₃Se 349.0343; found: 349.0349.
IR (neat) $\tilde{\nu}$ = 2850, 1756, 1725, 1650, 1626, 1565, 1024, 1015, 860, 735, 665 cm⁻¹.

Ethyl 3-oxo-2-(phenylselanyl)-3-(4-(trifluoromethyl)phenyl)propanoate (**3b**)

Batch: 33 mg, 0.08 mmol, 53%. Flow: 345 mg, 0.83 mmol, 67%.

¹H NMR (500 MHz, CDCl₃) δ = 7.93 (d, *J* = 8.1 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.58 – 7.55 (m, 2H), 7.41 – 7.24 (m, 3H), 5.29 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.2, 167.8, 137.9, 136.0, 134.75 (dd, *J* = 65.6, 32.8 Hz), 129.3, 129.3, 129.0, 127.2, 125.67 (q, *J* = 3.7 Hz), 62.5, 51.1, 14.0 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₈H₁₆O₃F₃Se 417.0217; found: 417.0219.

IR (neat) $\tilde{\nu}$ = 2846, 1856, 1730, 1734, 1645, 1526, 1134, 1067, 960, 765, 678 cm⁻¹.

Ethyl 3-(4-fluorophenyl)-3-oxo-2-(phenylselanyl)propanoate (**3c**)

Batch: 25 mg, 0.067 mmol, 45%. Flow: 282 mg, 0.77 mmol, 62%.

¹H NMR (300 MHz, CDCl₃) δ = 7.89 (dd, *J* = 9.0, 5.3 Hz, 2H), 7.64 – 7.55 (m, 2H), 7.40 – 7.24 (m, 3H), 7.07 (dd, *J* = 12.1, 5.3 Hz, 2H), 5.28 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.17 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (75 MHz, CDCl₃) δ = 189.4, 168.1, 167.7, 135.9, 131.55 (d, *J* = 9.4 Hz), 129.2, 129.1, 127.4, 115.87 (d, *J* = 22.0 Hz), 62.2, 51.5, 13.8 ppm.

HRMS (ES+) *m/z*: [M+Na]⁺ calcd for C₁₇H₁₆O₃FSe 367.0249; found: 367.0252.

IR (neat) $\tilde{\nu}$ = 2970, 1856, 1765, 1714, 1656, 1500, 1123, 1038, 932, 765, 545 cm⁻¹.

Ethyl 3-(4-bromophenyl)-3-oxo-2-(phenylselanyl)propanoate (**3d**)

Batch: 35 mg, 0.083 mmol, 55%. Flow: 341 mg, 0.8 mmol, 64%.

¹H NMR (500 MHz, CDCl₃) δ = 7.71 (dd, *J* = 8.9, 2.1 Hz, 2H), 7.58 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.57 – 7.52 (m, 2H), 7.39 – 7.26 (m, 3H), 5.25 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.1, 168.0, 135.9, 133.8, 131.9, 130.2, 129.3, 129.1, 128.9, 127.3, 62.4, 51.3, 13.8 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₇H₁₆O₃BrSe 426.9448; found: 426.9445.

IR (neat) $\tilde{\nu}$ = 2876, 1878, 1745, 1654, 1630, 1564, 1256, 1165, 934, 752, 645, 543 cm⁻¹.

Ethyl 3-(4-chlorophenyl)-3-oxo-2-(phenylselanyl)propanoate (**3e**)

Batch: 31 mg, 0.08 mmol, 53%. Flow: 336 mg, 0.88 mmol, 70%.

¹H NMR (300 MHz, CDCl₃) δ = 7.79 (d, *J* = 8.8 Hz, 2H), 7.62 – 7.55 (m, 2H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.35 – 7.27 (m, 3H), 5.26 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 189.9, 168.1, 140.2, 135.9, 133.4, 130.2, 129.3, 129.1, 129.0, 127.3, 62.4, 51.3, 13.9 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₇H₁₆O₃ClSe 382.0332; found: 382.0334

IR (neat) $\tilde{\nu}$ = 2848, 1878, 1724, 1722, 1625, 1589, 1326, 1181, 831, 754, 623 cm⁻¹.

Ethyl 3-(4-methoxyphenyl)-3-oxo-2-(phenylselanyl)propanoate (**3f**)

Batch: 33 mg, 0.086 mmol, 57%. Flow: 359 mg, 0.95 mmol, 76%.

¹H NMR (500 MHz, CDCl₃) δ = 7.85 (d, *J* = 9.0 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.35 – 7.23 (m, 3H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.29 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (75 MHz, CDCl₃) δ = 189.2, 168.9, 163.7, 135.8, 131.2, 129.2, 128.9, 128.0, 127.7, 113.9, 62.2, 55.6, 51.6, 13.8 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₈H₁₈O₄Se 379.0449; found: 379.0451.

IR (neat) $\tilde{\nu}$ = 2989, 1754, 1725, 1649, 1558, 1547, 1237, 1069, 786, 732, 640 cm⁻¹.

Ethyl 3-(4-*tert*-butylphenyl)-3-oxo-2-(phenylselanyl)propanoate (**3g**)

Batch: 33 mg, 0.082 mmol, 55%. Flow: 303 mg, 0.75 mmol, 60%.

¹H NMR (300 MHz, CDCl₃) δ = 7.81 (d, *J* = 8.7 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.42 (d, *J* = 8.7 Hz, 2H), 7.37 – 7.22 (m, 3H), 5.33 (s, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.32 (s, 9H), 1.16 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.5, 168.3, 157.5, 135.8, 132.5, 129.2, 128.9, 128.8, 127.8, 125.6, 62.2, 51.8, 34.9, 30.8, 13.9 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₂₁H₂₀O₃Se 405.0969; found: 405.0972.

IR (neat) $\tilde{\nu}$ = 2890, 1854, 1825, 1650, 1634, 1565, 1422, 1153, 864, 725, 649 cm⁻¹.

Ethyl 3-oxo-2-(phenylselanyl)-3-(*p*-tolyl)propanoate (**3h**)

Batch: 24 mg, 0.067 mmol, 45%. Flow: 272 mg, 0.75 mmol, 60%.

¹H NMR (500 MHz, CDCl₃) δ = 7.78 (d, *J* = 8.2 Hz, 2H), 7.64 – 7.59 (m, 2H), 7.36 – 7.26 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.32 (s, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.6, 168.4, 144.7, 136.5, 135.2, 130.0, 129.8, 129.5, 128.5, 128.3, 128.3, 62.2, 52.3, 51.2, 14.4 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₈H₁₈O₃Se 363.0499; found: 363.0500.

IR (neat) $\tilde{\nu}$ = 2834, 1855, 1725, 1676, 1645, 1448, 1256, 1173, 851, 735, 687 cm⁻¹.

Ethyl 3-([1,1'-biphenyl]-4-yl)-3-oxo-2-(phenylselanyl)propanoate (**3i**)

Batch: 30 mg, 0.07 mmol, 47 %. Flow: 327 mg, 0.77 mmol, 62%.

¹H NMR (300 MHz, CDCl₃) δ = 7.94 (d, *J* = 8.7 Hz, 2H), 7.66 – 7.59 (m, 5H), 7.51 – 7.44 (m, 2H), 7.44 – 7.37 (m, 2H), 7.37 – 7.24 (m, 3H), 5.37 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 190.6, 168.5, 146.4, 139.6, 135.9, 133.8, 129.4, 129.2, 129.1, 129.0, 128.4, 127.2, 62.2, 51.7, 13.8 ppm.

IR (neat) $\tilde{\nu}$ = 2832, 1835, 1730, 1663, 1630, 1575, 1210, 1179, 910, 733, 650 cm⁻¹.

Ethyl 3-(3-fluorophenyl)-3-oxo-2-(phenylselanyl)propanoate (**3j**)

Batch: 29 mg, 0.08 mmol, 53%. Flow: 326 mg, 0.89 mmol, 71%.

¹H NMR (500 MHz, CDCl₃) δ = 7.60 – 7.54 (m, 1H), 7.53 – 7.48 (m, 1H), 7.39 – 7.28 (m, 1H), 7.27 – 7.18 (m, 2H), 5.23 (s, 1H), 4.15 (q, *J* = 7.1 Hz, 1H), 1.14 (t, *J* = 7.1 Hz, 1H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 189.88 (d, *J* = 2.3 Hz), 167.9, 162.73 (d, *J* = 248.6 Hz), 137.21 (d, *J* = 6.4 Hz), 136.0, 130.32 (d, *J* = 7.7 Hz), 129.3, 129.2, 127.3, 124.50 (d, *J* = 3.0 Hz), 120.70 (d, *J* = 21.5 Hz), 115.60 (d, *J* = 22.8 Hz), 62.3, 51.2, 13.8 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₇H₁₆O₃FSe 367.0247; found: 367.0252.

IR (neat) $\tilde{\nu}$ = 2932, 1853, 1743, 1653, 1643, 1645, 1356, 1093, 950, 834, 650 cm⁻¹.

Ethyl 3-(3-bromophenyl)-3-oxo-2-(phenylselanyl)propanoate (**3k**)

Batch: 28 mg, 0.066 mmol, 44%. Flow: 354 mg, 0.83 mmol, 66%.

¹H NMR (300 MHz, CDCl₃) δ = 7.93 (t, *J* = 1.8 Hz, 1H), 7.76 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.67 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.36 (dd, *J* = 7.9, 2.2 Hz, 1H), 7.33 – 7.27 (m, 3H), 5.25 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm.

¹³C {¹H} NMR (126 MHz, CDCl₃) δ = 189.5, 167.8, 136.9, 136.4, 136.0, 131.7, 130.1, 129.3, 129.3, 127.2, 122.9, 62.2, 51.3, 13.8 ppm.

HRMS (ES+) *m/z*: [M+H]⁺ calcd for C₁₇H₁₆O₃BrSe 426.9448; found: 426.9447.

IR (neat) $\tilde{\nu}$ = 2857, 1846, 1735, 1652, 1636, 1576, 1130, 1123, 866, 745, 650 cm⁻¹.

Ethyl 3-(3-methoxyphenyl)-3-oxo-2-(phenylselanyl)propanoate (**3l**)

Batch: 31 mg, 0.083 mmol, 55%. Flow: 374 mg, 0.99 mmol, 79%.

^1H NMR (500 MHz, CDCl_3) δ = 7.61 (dd, J = 8.2, 1.3 Hz, 2H), 7.43 – 7.39 (m, 2H), 7.37 – 7.32 (m, 1H), 7.31 – 7.26 (m, 3H), 7.13 – 7.08 (m, 1H), 5.31 (s, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.81 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H) ppm.

^{13}C { ^1H } NMR (126 MHz, CDCl_3) δ = 190.8, 168.0, 159.7, 136.4, 135.9, 129.6, 129.2, 129.0, 127.6, 121.3, 120.5, 112.7, 62.2, 55.6, 51.8, 13.9 ppm.

HRMS (ES+) m/z : [$\text{M}+\text{H}$] $^+$ calcd for $\text{C}_{18}\text{H}_{19}\text{O}_4\text{Se}$ 379.0449; found: 379.0451.

IR (neat) $\tilde{\nu}$ = 2754, 1767, 1730, 1634, 1615, 1460, 1120, 1029, 890, 745, 676 cm^{-1} .

- (30) Boruah, T.; Arepally, S.; Melen, R. L.; Wirth, T. Numbering-Up Flow Electroreduction of α,β -Unsaturated Carbonyls from Gram to Pilot-Relevant Scale. *Org. Process Res. Dev.* **2026**, *30*, 2067–2074.



