Automated Electrochemical Selenenylations

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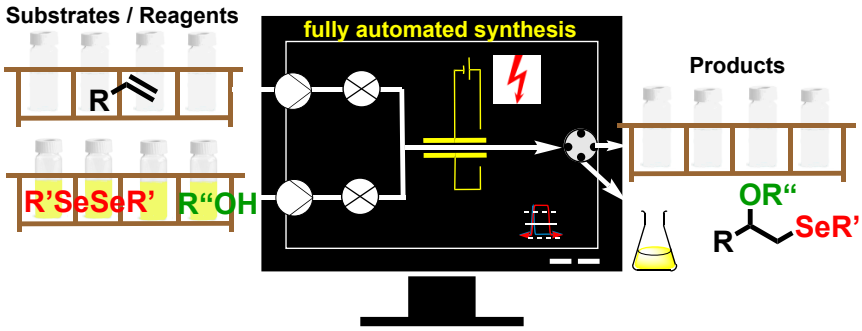

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Abstract: Integrated electrochemical reactors in automated flow systems have been utilised for selenenylation reactions. The automation has allowed to perform multiple electrochemical reactions of a programmed sequence in a fully autonomous way. Many functionalised selenenylated products have been synthesised in short reaction time with good to high yields.

Key words Alkenes, Automated synthesis, Electrolysis, Flow microreactors, Selenium

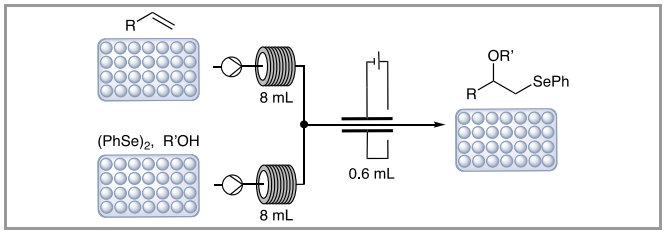


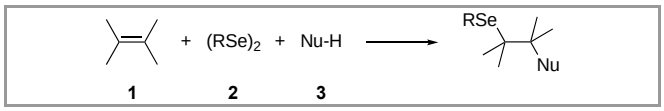
Figure 1. Automated selenenylations in flow electrochemistry.

There has been large efforts in developing technologies in organic synthesis to enhance product output in shorter time.[1] Continuous flow syntheses[2] and electrochemical reactions[3] have played a significant role in this development. These areas of research are still actively pursued in academia and industry. We have designed and manufactured an electrochemical flow microreactor device to improve the efficiency of electrochemical flow reactions integrated with inline mass spectrometric analysis. [4] A much improved device is now commercially available.[5] The advantage of being able to remotely control flow electrochemical equipment is demonstrated here with its inclusion in a fully automated flow setup. In continuation of our efforts in the development of tools and techniques we apply electrochemistry in the selenenylation of alkenes as a modular reaction. In the automated setup, the starting alkene, the diselenide as selenenylating reagent and the nucleophile can be selected. Different combinations will lead to different product solutions, which can be collected separately. The automated sequence of different reactions with integrated cleaning cycles allows an independent operation of many reactions, which is only limited by the number of available collection vials. A schematic representation of this system is shown in Figure 1. Automation has the potential to reduce the necessary manpower, avoiding human errors, and has a positive contribution towards sustainable and green chemistry by minimizing waste.[6]

Organoselenium compounds are interesting molecules owing to their importance in medicinal chemistry, material chemistry and as reagents and catalysts.[7] We have investigated many different aspects of selenium chemistry in the past including some batch electrochemical transformations. [8] Addition of selenium electrophiles to alkenes in the presence of nucleophiles is a general concept to access β-substituted selenides utilizing different reaction conditions and types of oxidants to access the selenium electrophiles. As an efficient and environmentally friendly protocol for organic synthesis, electrochemical conversions have gained more and more attention as often an excess amount of conventional chemical oxidants and reducing reagents can be avoided. [9] The synthesis of β-substituted selenides electrochemically is a very promising approach as shown also in recent publications.[10] These methods are efficient but still require a lot of effort to develop robust reliable reaction conditions. We describe the use of an automated electrochemical flow system for the synthesis of different β-substituted selenides in a continuous process. To the best of our knowledge, this is the first use of a flow electrochemical reactor integrated in an automated system.

We initiated our studies to identify optimal reaction conditions in the three component reaction using alkenes, diphenyl diselenide and different alcohols as nucleophiles (Scheme 1). We use a Vapourtec automated flow system with the integrated Ion electrochemical microflow reactor to rapidly and automatically

screen different reaction variables. The software allowed a setup of a number of reactions applying different reaction conditions and collecting the individual reaction products in an automated way even during overnight operation.



Scheme 1. Selenenylation of alkenes.

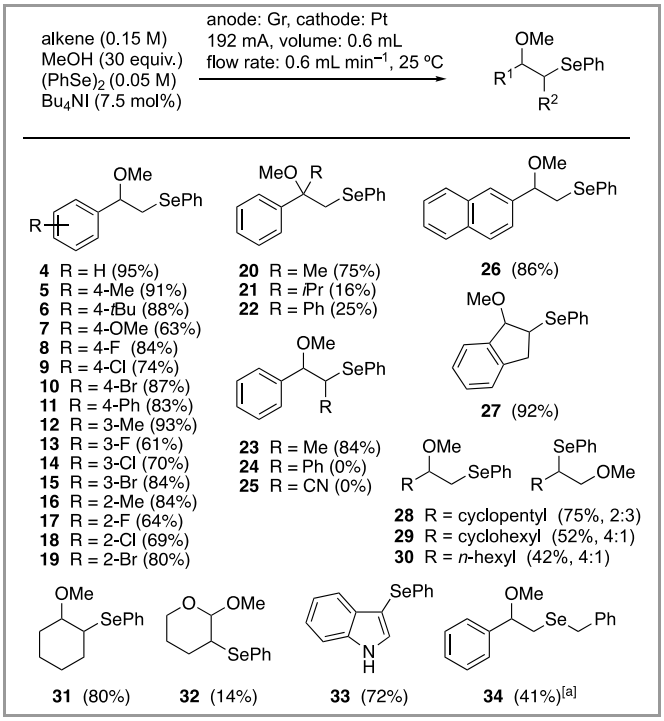
As a model reaction, styrene (0.15 M), diphenyl diselenide (0.05 M) and CH_3OH (30 equiv) in CH_3CN were reacted using graphite (Gr) as anode and platinum (Pt) as cathode with a flow rate of 0.1 mL min^{-1} and 5 mM tetrabutylammonium tetrafluoroborate (Bu_4NBF_4) as the supporting electrolyte. With a residence time of 6 minutes and a current of 16 mA (2.0 F) at room temperature, only 32% of the desired product **4** was obtained. Theoretically, only 2.0 F electricity is required for the two-electron oxidation. However, it was observed that increasing current from 16 mA to 32 mA (4 F) increases the yield from 32% to 66% with recovery of starting materials. A further increase of the current beyond 4.0 F led to a decrease of the yield of the desired product **4**.

Different parameters for the flow electrochemical reactions were studied such as solvents, electrolytes, flow rates and electrode materials. Different solvents and solvent mixtures such as acetonitrile, tetrahydrofuran, methanol and mixtures of acetonitrile/tetrahydrofuran were screened. It was found that acetonitrile was the optimal solvent for this reaction (see supporting information). Lei and co-authors reported an oxyselenenylation using styrene in a batch electrochemical process using stoichiometric amounts of tetrabutylammonium tetrafluoroborate (Bu_4NBF_4) as a supporting electrolyte.[10b] We discovered that under flow conditions only catalytic amounts of Bu_4NBF_4 were necessary to obtain identical results in a shorter reaction time. Without any addition of electrolyte, the reaction in the electrochemical flow reactor still led to a yield of 32%. The presence of electrolyte has a significant influence on the yield. Different electrolytes such as Bu_4NBF_4, Bu_4NOTs, Et_4NCl, Bu_4NBr, KI and Bu_4NI were screened in catalytic amounts and Bu_4NI showed the highest yield of 87% (see supporting information). From cyclic voltammetry studies (see supporting information) we presume that iodide is oxidised at the anode sequentially from iodide to the iodine radical to iodine cation: $I^- \rightarrow I^\bullet \rightarrow I^+$.[10c] The iodine cation is known to activate the diselenide by generating PhSeI and another reactive $PhSe^+$ that reacts to the desired product.

The effect of flow rate/residence time on product yield were studied as to determine the optimal flow rate in order to avoid mass-transfer limitations.[11] Surprisingly, increasing the flow rate to 0.2 - 0.4 mL min^{-1} led to full conversion with >99% yield. A further increase to flow rates above 0.4 mL min^{-1} resulted in a drop in yield. It may be due to a decreased conductivity at higher flow rates. An increase of the electrolyte concentration from 5 mM to 7.5 mM allowed to obtain again quantitative yield at flow rates up to 0.6 mL min^{-1} corresponding to a calculated residence time of 1.0 minutes (see supporting information). Due to the formation of hydrogen the actual residence time is lower. The increase in electrolyte concentration allowed a further reduction of the reaction time.

Also different electrode materials were screened[4] (see supporting information). Initially, platinum (Pt) was used as cathode and different anode materials such as graphite (Gr), glassy carbon (GC), boron-doped diamond (BDD), Panasonic carbon, PTFE carbon, stainless steel (Fe) and nickel (Ni) were screened. Among these, Gr as anode was found to be most efficient. Furthermore, Gr as anode was then screened against various cathodes such as Pt loaded on Nb, Pt loaded on Ti, Ni, Fe, Gr, GC and Zn. From this screening it was found that Gr as anode and Pt as cathode were an optimal combination. A low-cost electrode (Pt loaded on Nb) still gave 95% yield. The same trend was observed for Gr as a cathode and anode.

With the optimised reaction conditions in hand, an investigation of the scope and general applicability of this methodology using different alkenes, alcohols and diselenides was performed in an automated way. Loading different alkenes, alcohols and diselenides into the autosampler allowed the reaction products shown in Schemes 2, 3 and Figure 2 to be obtained in a fully automated way without additional manual interference. The different product solutions obtained were purified using a Biotage Isolera chromatography system. Due to the automated protocol, all reactions shown have been performed using identical amounts and concentrations of reagents and 1.2 mmol alkene have been used in each experiment.

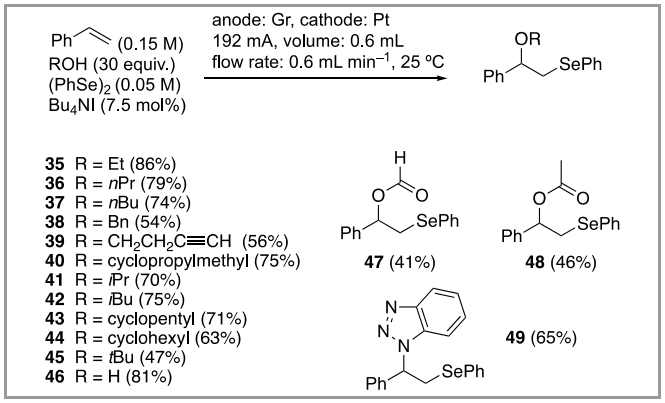


Scheme 2. Scope and limitation for electrochemical methoxyselenenylations of alkenes. [a] Dibenzyl diselenide used instead of diphenyl diselenide.

Pleasingly, the electrochemical reaction of many different substituted styrene derivatives gave the desired products **4** – **27** in good to excellent yields except for **24** and **25**, where the disubstituted alkenes did not lead to any product formation. Alkyl-substituted alkenes lead, as known, to regioisomeric mixtures (**28** – **30**). While 3,4-dihydro-2*H*-pyran formed product **32** in 14% yield as the only regioisomer but, as reported, in a 1:1 (*cis:trans*) mixture,[12] indole was selenenylated in the 3-position leading to **33**.[13] Also other diselenides such as dibenzyl

diselenide can be used as demonstrated in the synthesis of **34,** where CH_3CN and THF as a solvent mixture (1:1) were used.

Variations of nucleophiles in the selenenylation are shown in Scheme 3. Primary, secondary and tertiary alcohols can be used in the selenenylation reactions as shown in the formation of products **35** – **45**. Even water, formic acid and acetic acid can be used and products **46** – **48** are obtained. Benzotriazole as an *N*-nucleophile participated in this reaction to form the aminoselenenylated product **49** in 65% yield.



Scheme 3. Different nucleophiles for the electrochemical selenenylation of styrene.

Cyclic ethers and lactones are important cores in several natural products and important bioactive molecules. This methodology can also be expanded to intramolecular cyclizations and was found to be efficient to obtain a variety of cyclised *O*-heterocycles as shown in Figure 2. The lactones and ethers were obtained in moderate to good yields. Furan such as **50** was obtained in 73% yield. Functionalised pyrans **51** and **52** were obtained in 67 and 58% yield, respectively. Different functionalised and fused lactones **53** – **56** were obtained in good yields. Similarly, dihydroindole **57** was synthesised and was obtained in 33% yield. All the synthesised compounds were fully characterised using different spectroscopic techniques. Among them, also a single crystal x-ray analysis was performed for compound **21** (see supporting information) that further supports the formation of the target molecules and the spectroscopic data. [14] The selenium cation necessary for the addition and cyclisation reactions described here is believed to be formed through sequential oxidation of diphenyl diselenide as already investigated by Breder, Siewert and coworkers.[10d] The oxidation potential required for a subsequent elimination of the selenide is not reached here.

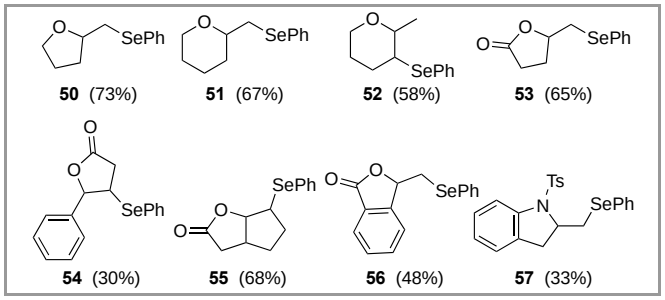


Figure 2. Electrochemical selenocyclisations.

To further demonstrate the synthetic potential of this protocol, a gram scale reaction was performed for the synthesis of product **4**. 1.52 g of **4** was synthesised in 100 minutes corresponding to 87% yield.

In summary, we have demonstrated that electrochemical reactions such as selenenylations of alkenes can be easily integrated in remote-controlled synthesis equipment allowing an automated synthesis of many derivatives in a short time with minimal human interference. A library of 54 molecules of alkoxy and aza-selenenylations have been synthesised including intramolecular reactions for the synthesis of heterocyclic compounds. A gram scale reaction was also performed to demonstrate the potential of this electrochemically integrated automated flow technology.

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All solvents and reagents were used as received without purification or drying. Thin-layer chromatography (TLC) was performed on pre-coated aluminium sheets of Merck silica gel 60 F254 (0.20 mm) and visualised by UV radiation (254 nm). Automated column chromatography was performed on a Biotage® Isolera Four using Biotage® cartridges SNAP Ultra 10 g. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were measured on Bruker DPX 400 or 500 apparatus and were referenced to the residual proton solvent peak (^{1}H: $CDCl_3$, δ 7.26 ppm; DMSO-d_6, δ 2.50 ppm) and solvent ^{13}C signal ($CDCl_3$, δ 77.2 ppm, DMSO-d_6, δ 39.5). Chemical shifts δ were reported in ppm, multiplicity of the signals was declared as followed: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, hep = septet, dd = doublet of doublets, m = multiplet, b = broad; and coupling constants (*J*) in Hertz. IR spectra were recorded on a Shimadzu FTIR Affinity-1S apparatus. Wavenumbers are quoted in cm^{-1}. All compounds were measured neat directly on the crystal of the IR machine. Mass spectrometric measurements were performed by R. Jenkins, R. Hick, T. Williams and S. Waller at Cardiff University on a Water LCR Premier XEtof. Ions were generated by Electron Ionisation (EI) and Electron Spray (ES). The molecular ion peaks values quoted for either molecular ion $[M]^+$, molecular ion plus hydrogen $[M+H]^+$ or molecular ion plus sodium $[M+Na]^+$. Melting points were measured using a Gallenkamp variable heater with samples in open capillary tubes. The electrochemical reactions were carried out in a galvanostatic mode using a Vapourtec Ion Electrochemical flow reactor[5] powered by an Ion electrochemical power supply. The cyclic voltammograms (SI) were performed using an Orygalys OGF500 Potentiostat / Galvanostat with OGFPWR power supply.

General procedure for electrochemical oxyselenenylations of alkenes (GP1):

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 a Graphite (Gr) electrode as the anode and a platinum (Pt) electrode as the cathode (active surface area: 2 x 12 cm^2). A solution of alkene (0.15 M in CH_3CN) placed in vial A and mixture of diphenyl diselenide (0.05 M), alcohol (30 equiv) and TBAI (0.0075 M) in CH_3CN was placed in vial B. Each solution was injected into an 8 mL sample loop. After that, the reactor temperature was set at 25 ºC with the flow rate 0.6 mL/min and the current was set at 192 mA to turn on automatically. Then, both solutions were pumped into a PTFE coil (1 mm internal diameter) and mixed *via* a T-piece connected to a 30 cm PTFE coil before the inlet of the electrochemical rector. After reaching a steady state, the solution (12 mL) was collected automatically into a collection glass vial. The solvent was removed under vacuum. The crude product was purified by column chromatography (EtOAc/hexane).

General procedure for electrochemical selenocyclisations (GP2):

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 a Graphite (Gr) electrode as the anode and a platinum (Pt) electrode as the cathode (immersed surface area: A = 12 cm^2). A solution of alkene (0.15 M in CH_3CN) place in vial A and mixture of diphenyl diselenide (0.05 M) and TBAI (0.0075 M) in CH_3CN was placed in vial B. Each solution was injected to 8 ml sample loop. After that, the reactor temperature was set at 25 °C with the flow rate 0.6 mL/min and the current set at 192 mA turn

on automatically. Then, both solutions were pumped into a PTFE coil (1 mm internal diameter) and mix via a T-piece connected to 30 cm PTFE coil before the inlet of the electrochemical rector. After reaching a steady state, the solution (12 mL) was collected automatically into a collection glass vial. The solvent was removed under vacuum. The crude product was purified by column chromatography (EtOAc/hexane).

(2-Methoxy-2-phenylethyl)(phenyl)selane (4)

Compound **4** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 165 mg (95% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.45 (m, 2H), 7.38 – 7.29 (m, 5H), 7.26 – 7.22 (m, 3H), 4.35 (dd, *J* = 8.4, 5.0 Hz, 1H), 3.33 (dd, *J* = 12.3, 8.4 Hz, 1H), 3.25 (s, 3H), 3.11 (dd, *J* = 12.3, 5.0 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.0, 132.7, 130.8, 129.2, 128.7, 128.2, 126.9, 126.8, 83.3, 57.2, 35.5 ppm

(2-Methoxy-2-(*p*-tolyl)ethyl)(phenyl)selane (5)

Compound **5** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 167 mg (91% yield). The spectral data are in agreement with literature.[15]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 – 7.44 (m, 2H), 7.26 – 7.14 (m, 7H), 4.33 (dd, *J* = 8.4, 5.1 Hz, 1H), 3.33 (dd, *J* = 12.2, 8.4 Hz, 1H), 3.24 (s, 3H), 3.10 (dd, *J* = 12.2, 5.1 Hz, 1H), 2.36 (s, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.7, 132.6, 130.9, 129.4, 129.1, 126.9, 126.8, 83.1, 57.0, 35.5, 21.3 ppm

(2-(4-(*tert*-Butyl)phenyl)-2-methoxyethyl)(phenyl)selane (6)

Compound **6** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to obtain 184 mg (88% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 – 7.43 (m, 2H), 7.40 – 7.38 (m, 2H), 7.26 – 7.18 (m, 5H), 4.35 (dd, *J* = 8.5, 4.9 Hz, 1H), 3.33 (dd, *J* = 12.3, 8.5 Hz, 1H), 3.25 (s, 3H), 3.11 (dd, *J* = 12.3, 4.9 Hz, 1H), 1.32 (s, 9H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.2, 138.0, 132.7, 130.9, 129.1, 126.9, 126.5, 125.5, 83.3, 57.2, 35.5, 34.7, 31.6 ppm

(2-Methoxy-2-(4-methoxyphenyl)ethyl)(phenyl)selane (7)

Compound **7** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 122 mg (63% yield). The spectral data are in agreement with literature.[15]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 – 7.43 (m, 2H), 7.26 – 7.20 (m, 5H), 6.89 – 6.82 (m, 2H), 4.31 (dd, *J* = 8.2, 5.3 Hz, 1H), 3.81 (s, 3H), 3.33 (dd, *J* = 12.2, 8.3 Hz, 1H), 3.22 (s, 3H), 3.09 (dd, *J* = 12.2, 5.3 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.6, 133.0, 132.6, 130.9, 129.1, 128.0, 126.9, 114.0, 82.8, 56.9, 55.4, 35.5 ppm

(2-(4-Fluorophenyl)-2-methoxyethyl)(phenyl)selane (8)

Compound **8** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 156 mg (84% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.42 (m, 2H), 7.29 – 7.20 (m, 5H), 7.07 – 6.97 (m, 2H), 4.33 (dd, *J* = 8.0, 5.5 Hz, 1H), 3.30 (dd, *J* = 12.3, 8.0 Hz, 1H), 3.23 (s, 3H), 3.07 (dd, *J* = 12.3, 5.5 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.6 (d, *J* = 243.7 Hz), 136.7 (d, *J* = 3.7 Hz), 132.8, 129.2, 128.4 (d, *J* = 8.7 Hz), 127.0, 115.5 (d, *J* = 22.5 Hz), 82.7, 56.1, 35.4 ppm

(2-(4-Chlorophenyl)-2-methoxyethyl)(phenyl)selane (9)

Compound **9** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 144 mg (74% yield). The spectral data are in agreement with literature.[15]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 – 7.44 (m, 2H), 7.32 – 7.28 (m, 2H), 7.26 – 7.16 (m, 5H), 4.31 (dd, *J* = 7.9, 5.5 Hz, 1H), 3.29 (dd, *J* = 12.3, 8.0 Hz, 1H), 3.23 (s, 3H), 3.06 (dd, *J* = 12.3, 5.5 Hz, 1H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.5, 133.9, 132.8, 130.5, 129.2, 128.9, 128.2, 127.1, 82.7, 57.2, 35.2 ppm

(2-(4-Bromophenyl)-2-methoxyethyl)(phenyl)selane (10)

Compound **10** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) to obtain 194 mg (87% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 – 7.43 (m, 4H), 7.26 – 7.20 (m, 3H), 7.18 – 7.14 (m, 2H), 4.30 (dd, *J* = 7.9, 5.5 Hz, 1H), 3.28 (dd, *J* = 12.4, 7.9 Hz, 1H), 3.23 (s, 3H), 3.06 (dd, *J* = 12.4, 5.5 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.0, 132.9, 131.8, 130.5, 129.2, 128.9, 127.1, 122.1, 82.7, 57.2, 35.2 ppm

(2-([1,1'-Biphenyl]-4-yl)-2-methoxyethyl)(phenyl)selane (11)

Compound **11** was synthesised following GP1 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 184 mg (83% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 – 7.57 (m, 4H), 7.50 –7.44 (m, 4H), 7.39 – 7.34 (m, 3H), 7.26 – 7.22 (m, 3H), 4.41 (dd, *J* = 8.3, 5.2 Hz, 1H), 3.37 (dd, *J* = 12.3, 8.3 Hz, 1H), 3.30 (s, 3H), 3.15 (dd, *J* = 12.3, 5.2 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.2, 140.9, 140.0, 132.8, 130.8, 129.1, 128.9, 127.4, 127.4, 127.2, 127.2, 126.9, 83.1, 57.2, 35.5 ppm

IR (neat): 3055, 2819, 1485, 1477, 1085, 732, 692 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{20}H_{17}Se[M–OMe]^+$: 333.0522, found: 333.0525

(2-Methoxy-2-(*m*-tolyl)ethyl)(phenyl)selane (12)

Compound **12** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 170 mg (93% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.44 (m, 2H), 7.26 – 7.20 (m, 4H), 7.12 – 7.09 (m, 3H), 4.32 (dd, *J* = 8.5, 5.0 Hz, 1H), 3.32 (dd, *J* = 12.2, 8.5 Hz, 1H), 3.25 (s, 3H), 3.10 (dd, *J* = 12.2, 5.0 Hz, 1H), 2.35 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.0, 138.4, 132.7, 130.9, 129.1, 129.0, 128.6, 127.4, 126.9, 123.9, 83.4, 57.2, 35.5, 21.6 ppm

IR (neat): 2981, 2820, 1477, 1437, 1084, 731 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{15}H_{15}Se[M–OMe]^+$: 271.0366, found: 271.0374

(2-(3-Fluorophenyl)-2-methoxyethyl)(phenyl)selane (13)

Compound **13** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 114 mg (61% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.44 (m, 2H), 7.32 – 7.25 (m, 1H), 7.24 – 7.21 (m, 3H), 7.09 – 6.96 (m, 3H), 4.33 (dd, *J* = 8.1, 5.2 Hz, 1H), 3.29 (dd, *J* = 12.4, 8.2 Hz, 1H), 3.26 (s, 3H), 3.08 (dd, *J* = 12.4, 5.2 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 163.2 (d, *J* = 245.0 Hz), 143.9 (d, *J* = 6.2 Hz), 132.9, 130.5, 130.2 (d, *J* = 7.5 Hz), 129.2, 127.1, 122.5 (d, *J* = 2.5 Hz), 115.1 (d, *J* = 21.2 Hz), 113.7 (d, *J* = 25.0 Hz), 113.52, 82.8 (d, *J* = 2.5 Hz), 57.3, 35.2 ppm

^{19}F NMR (471 MHz, $CDCl_3$): δ = –112.69 (s) ppm

IR (neat): 2932, 2822, 1477, 1436, 1089, 1072, 733 cm^{-1}

(2-(3-Chlorophenyl)-2-methoxyethyl)(phenyl)selane (14)

Compound **14** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 138 mg (70% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 – 7.43 (m, 2H), 7.29 – 7.27 (m, 1H), 7.27 – 7.21 (m, 5H), 7.19 – 7.14 (m, 1H), 4.30 (dd, *J* = 8.1, 5.3 Hz, 1H), 3.27 (dd, *J* = 12.4, 8.1 Hz, 1H), 3.24 (s, 3H), 3.06 (dd, *J* = 12.4, 5.3 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.2, 134.7, 133.0, 130.5, 130.0, 129.2, 128.4, 127.1, 127.0, 125.0, 82.8, 57.4, 35.2 ppm

IR (neat): 2986, 2821, 1475, 1437, 1099, 1074, 733 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{14}H_{12}ClSe[M–OMe]^+$ 290.9820, found: 290.9810

(2-(3-Bromophenyl)-2-methoxyethyl)(phenyl)selane (15)

Compound **15** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 187 mg (84% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 – 7.40 (m, 4H), 7.26 – 7.18 (m, 5H), 4.30 (dd, *J* = 8.1, 5.3 Hz, 1H), 3.28 (dd, *J* = 12.4, 8.1 Hz, 1H), 3.25 (s, 3H), 3.06 (dd, *J* = 12.4, 5.3 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.5, 132.9, 131.3, 130.4, 130.3, 129.9, 129.2, 127.2, 125.5, 122.9, 82.8, 57.4, 35.2 ppm

IR (neat): 2984, 2819, 1476, 1436, 1082, 1070, 732, 688 cm^{-1}

(2-Methoxy-2-(o-tolyl)ethyl)(phenyl)selane (16)

Compound **16** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 154 mg (84% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 – 7.50 (m, 2H), 7.40 – 7.38 (m, 1H), 7.25 – 7.11 (m, 6H), 4.60 (dd, *J* = 9.0, 4.2 Hz, 1H), 3.31 – 3.17 (m, 4H), 3.07 (dd, *J* = 12.5, 4.2 Hz, 1H), 2.22 (s, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.1, 135.7, 133.2, 130.7, 130.6, 129.1, 127.8, 127.1, 126.5, 126.0, 79.7, 57.1, 34.7, 19.1 ppm

IR (neat): 2980, 2820, 1477, 1437, 1022, 729 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{15}H_{15}Se[M–OMe]^+$: 271.0366, found: 271.035

(2-(2-Fluorophenyl)-2-methoxyethyl)(phenyl)selane (17)

Compound **17** was synthesised following GP1 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 120 mg (64% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 – 7.48 (m, 2H), 7.44 – 7.40 (m, 1H), 7.29 – 7.22 (m, 4H), 7.18 – 7.14 (m, 1H), 7.04 – 7.00 (m, 1H), 4.75 (dd, *J* = 8.2, 4.9 Hz, 1H), 3.32 – 3.25 (m, 4H), 3.20 (dd, *J* = 12.7, 4.6 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 160.5 (d, *J* = 245.0 Hz), 132.8, 130.6, 129.5 (d, *J* = 8.7 Hz), 129.1, 128.0 (d, *J* = 13.7 Hz), 127.7 (d, *J* = 3.7 Hz), 127.0, 124.5 (d, *J* = 3.7 Hz), 115.5 (d, *J* = 22.5 Hz), 76.6 (d, *J* = 1.3 Hz), 57.5, 34.1 ppm

^{19}F NMR (471 MHz, $CDCl_3$) δ = –119.2 ppm

IR (neat): 3086, 2824, 1477, 1436, 1105, 1088, 734 cm^{-1}

(2-(2-Chlorophenyl)-2-methoxyethyl)(phenyl)selane (18)

Compound **18** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 134 mg (69% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 – 7.49 (m, 3H), 7.34 – 7.28 (m, 2H), 7.26 – 7.19 (m, 4H), 4.85 (dd, *J* = 8.7, 3.9 Hz, 1H), 3.29 (s, 3H), 3.23 (dd, *J* = 12.5, 3.9 Hz, 1H), 3.16 (dd, *J* = 12.5, 8.7 Hz, 1H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.6, 133.2, 133.1, 130.6, 129.7, 129.1, 127.4, 127.4, 127.0, 79.3, 57.6, 34.1 ppm

IR (neat): 2985, 2823, 1475, 1436, 1072.1034, 733 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{14}H_{12}ClSe[M–OMe]^+$: 290.9820, found: 290.9812

(2-(2-Bromophenyl)-2-methoxyethyl)(phenyl)selane (19)

Compound **19** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 178 mg (80% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56 – 7.53 (m, 2H), 7.52 – 7.47 (m, 2H), 7.36 – 7.32 (m, 1H), 7.25 – 7.20(m, 3H), 7.16 – 7.13 (m, 1H), 4.79 (dd, *J* = 8.9, 3.7 Hz, 1H), 3.29 (s, 3H), 3.22 (dd, *J* = 12.6, 3.7 Hz, 1H), 3.13 (dd, *J* = 12.6, 8.9 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.5, 133.0, 131.3, 130.4, 130.3, 129.9, 129.2, 127.2, 125.5, 122.9, 82.8, 57.4, 35.2 ppm

IR (neat): 3055, 2824, 1475, 1435, 1072.1022, 732, 690 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{14}H_{12}BrSe[M–OMe]^+$ 334.9315, found: 334.9301

(2-Methoxy-2-phenylpropyl)(phenyl)selane (20)

Compound **20** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 138 mg (75% yield). The spectral data are in agreement with literature.[17]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 – 7.39 (m, 4H), 7.36 – 7.32 (m, 2H), 7.29 – 7.25 (m, 1H), 7.20 – 7.16 (m, 3H), 3.43 (d, *J* = 11.3 Hz, 1H), 3.28 (d, *J* = 11.8 Hz, 1H), 3.13 (s, 3H), 1.72 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.8, 132.8, 131.5, 129.0, 128.4, 127.5, 126.8, 126.4, 79.1, 51.2, 42.6, 23.3 ppm

(2-Methoxy-3-methyl-2-phenylbutyl)(phenyl)selane (21)

Compound **21** was synthesised following GP1 as a colourless solid. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 32 mg (16% yield).

m.p. = 87 – 88 ºC

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 – 7.55 (m, 2H), 7.36 – 7.24 (m, 8H), 3.79 (d, *J* = 12.0 Hz, 1H), 3.62 (d, *J* = 12.0 Hz, 1H), 3.26 (s, 3H), 2.41 (dt, *J* = 13.6, 6.8 Hz, 1H), 0.79 (d, *J* = 6.7 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.3, 133.3, 131.0, 129.2, 128.0, 127.6, 127.1, 127.1, 83.7, 50.9, 35.4, 34.8, 18.2, 16.9 ppm

IR (neat): 2966, 2818, 1471, 1170, 1070, 761, 744, 705, 690 cm^{-1}

(2-Methoxy-2,2-diphenylethyl)(phenyl)selane (22)

Compound **22** was synthesised following GP1 as a colourless solid. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 56 mg (25% yield). The spectral data are in agreement with literature.[18]

m.p. = 76 – 78 ºC

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44 – 7.34 (m, 6H), 7.33 – 7.28 (m, 4H), 7.26 – 7.17 (m, 5H), 3.96 (s, 2H), 3.16 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.3, 133.3, 130.9, 129.0, 128.1, 127.3, 127.1, 127.0, 82.2, 50.9, 37.9 ppm

(1-Methoxy-1-phenylpropan-2-yl)(phenyl)selane (23)

Compound **23** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 153 mg (84% yield). The spectral data are in agreement with literature.[19]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 – 7.53 (m, 2H), 7.38 – 7.22 (m, 8H), 4.41 (d, *J* = 4.5 Hz, 1H), 3.48 (qd, *J* = 7.0, 4.5 Hz, 1H), 3.30 (s, 3H), 1.35 (d, *J* = 7.1 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.8, 134.7, 130.1, 129.1, 128.4, 127.9, 127.5, 127.2, 86.5, 57.7, 45.9, 16.5 ppm

(2-Methoxy-2-(naphthalen-2-yl)ethyl)(phenyl)selane (26)

Compound **26** was synthesised following GP1 as a orange oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 177 mg (86% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 – 7.81 (m, 3H), 7.75 (s, 1H), 7.52 – 7.42 (m, 5H), 7.25 – 7.14 (m, 3H), 4.52 (dd, *J* = 8.3, 5.2 Hz, 1H), 3.40 (dd, *J* = 12.3, 4.0 Hz, 1H), 3.29 (s, 3H), 3.19 (dd, *J* = 12.3, 5.2 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.5, 134.4, 133.5, 133.4, 132.9, 130.8, 129.2, 128.8, 128.2, 127.9, 127.1, 126.5, 126.4, 126.3, 124.3, 83.6, 77.3, 57.3, 35.4 ppm

IR (neat): 3050, 2931, 1477, 1437, 1101, 1022, 735 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{18}H_{15}Se[M–OMe]^+$: 307.0366, found: 307.0359

(1-Methoxy-2,3-dihydro-1*H*-inden-2-yl)(phenyl)selane (27)

Compound **27** was synthesised following GP1 as a orange oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 168 mg (92% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 – 7.57 (m, 2H), 7.39 (d, *J* = 7.1 Hz, 1H), 7.32 – 7.19 (m, 6H), 4.76 (d, *J* = 2.8 Hz, 1H), 4.08 – 3.97 (m, 1H), 3.60 (dd, *J* = 17.0, 7.4 Hz, 1H), 3.36 (s, 3H), 2.94 (dd, *J* = 17.0, 3.7 Hz, 1H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.3, 140.9, 134.4, 129.6, 129.3, 129.1, 127.8, 127.0, 125.7, 125.3, 90.3, 57.0, 44.8, 38.4 ppm

(2-Cyclopentyl-2-methoxyethyl)(phenyl)selane (28a) and **(1-Cyclopentyl-2-methoxyethyl)(phenyl)selane (28b)**

Compounds **28a** and **28b** were synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 127 mg (75% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 – 7.56 (**a**; m, 3H), 7.54 – 7.51 (**b**; m, 2H), 7.28 – 7.20 (**a** + **b**; m, 8H), 3.59– 3.56 (**a** + **b**; m, 3H), 3.38 (**b**; s, 3H), 3.32 (**a**; s, 3H), 3.32 – 3.22 (**a** + **b**; m, 3H), 3.16 (**a**; dd, *J* = 12.3, 4.8 Hz, 1H), 3.08 (**a**; dd, *J* = 12.3, 5.8 Hz, 1H), 2.31 – 2.09 (**a** + **b**; m, 2.6H), 1.94 – 1.15 (**a** + **b**; m, 20H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.6, 132.7, 131.1, 130.10, 129.2, 129.1, 127.4, 126.9, 84.4, 75.71, 58.9, 58.0, 51.85, 44.3, 42.1, 31.7, 31.5, 31.2, 29.35, 28.7, 25.7, 25.6, 25.64, 25.38 ppm

IR (neat): 2947, 2866, 1577, 1475, 1436, 1095, 906, 729, 690 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{13}H_{17}Se[M–OMe]^+$: 249.0522, found: 249.0524.

(2-cyclohexyl-2-methoxyethyl)(phenyl)selane (29a) and **(1-cyclohexyl-2-methoxyethyl)(phenyl)selane (29b)**

Compound **29** was synthesised following the GP1 as pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 43% isolated yield (76 mg).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 – 7.51 (**a** + **b**; m, 3.6H), 7.29 – 7.20 (**a** + **b**; m, 6H), 3.68 (**a**; dd, *J* = 10.1, 8.5 Hz, 1H), 3.56 (**a**; dd, *J* = 10.1, 5.1 Hz, 1H), 3.38 (**b**; s, 3H), 3.30 (**a**; s, 3H), 3.26 – 3.22 (**a**; m, 1H), 3.21 – 3.03 (**a** + **b**; m, 2.5H), 1.89 – 1.40 (**a** + **b**; m, 12H), 1.35 – 1.05 (**a** + **b**; m, 8H) ppm

^{13}C NMR (126 MHz, $CDCl_3$); δ = 134.2, 132.7, 131.1, 130.5, 129.1, 129.1, 127.2, 126.8, 85.2, 74.0, 58.7, 58.3, 53.1, 41.4, 39.3, 31.7, 30.1, 30.0, 29.0, 28.3, 26.6, 26.5, 26.54, 26.4, 26.3 ppm

IR (neat): 2974, 2920, 2850, 1577, 1475, 1436, 1097, 1083, 1022, 734, 690 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{14}H_{19}Se[M–OMe]^+$ 263.0679, found: 263.0685.

(2-Methoxyoctyl)(phenyl)selane (30a) and **(1-Methoxyoctan-2-yl)(phenyl)selane (30b)**

Compounds **30a** and **30b** were synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 75 mg (42% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.44 (**a** + **b**; m, 2H), 7.20 – 7.14 (**a** + **b**; m, 4H), 3.48 (**b**; dd, *J* = 9.9, 5.2 Hz, 1H) , 3.42 (**b**; dd, *J* = 9.9, 7.5 Hz, 1H), 3.33 – 3.27 (**a**; m, 1H), 3.26 (**a**; s, 3H), 3.25 (**b**; s, 3H), 3.23 – 3.18 (**b**; s,1H), 3.03 (**a**; dd, *J* = 12.2, 5.5 Hz, 1H), 2.94 (**a**; dd, *J* = 12.2, 6.1 Hz, 1H), 1.58 – 1.13 (**a** + **b**; m, 12.5H), 0.80 (**a** + **b**; m, 3.75H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.9, 133.0, 132.8, 130.9, 129.2, 129.1, 127.6, 126.9, 80.6, 76.0, 58.8, 57.1, 45.0, 32.3, 32.1, 31.9, 31.8, 29.4, 29.2, 27.8, 25.4, 22.7, 14.2 ppm

IR (neat): 2926, 2854, 1577, 1477, 1436, 1091, 1074, 734, 690 cm^{-1}

(2-Methoxycyclohexyl)(phenyl)selane (31)

Compound **31** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 130 mg (80% yield). The spectral data are in agreement with literature.[20]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56-7.56 (m, 2H), 7.28 – 7.23 (m, 3H), 3.38 (s, 3H), 3.27 (m, 1H), 3.18 (m, 1H), 2.15 (m, 1H), 2.04 – 1.97 (m, 1H), 1.76 – 1.45 (m, 3H), 1.38 – 1.19 (m, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 135.5, 129.1, 128.9, 127.5, 82.4, 56.5, 47.5, 32.3, 30.4, 25.9, 23.6 ppm

2-Methoxy-3-(phenylselanyl)tetrahydro-2*H*-pyran (32)

Compound **32** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 23 mg (14% yield). The spectral data are in agreement with literature.[21]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 – 7.54 (m, 2H), 7.30 – 7.23 (m, 3H), 4.51 (d, *J* = 4.9 Hz, 1H), 3.90 (ddd, *J* = 11.2, 7.4, 3.6 Hz, 1H), 3.58 – 3.49 (m, 1H), 3.42 (s, 3H), 3.27 (dt, *J* = 7.4, 4.6 Hz, 1H), 2.20 (ddd, *J* = 16.9, 8.1, 3.9 Hz, 1H), 1.86 – 1.68 (m, 2H), 1.57 – 1.48 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 134.9, 129.1, 129.0, 127.7, 103.2, 62.9, 55.7, 44.2, 27.5, 24.4 ppm

1-Methyl-3-(phenylselanyl)-1*H*-indole (33)

Compound **33** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (9:1) to obtain 125 mg (72% yield). The spectral data are in agreement with literature.[22]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 – 7.55 (m, 1H), 7.31 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.26 – 6.95 (m, 8H), 3.78 (s, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.6, 135.8, 134.4, 130.8, 129.0, 128.8, 125.6, 122.6, 120.6, 120.6, 109.7, 96.1, 33.2 ppm

Benzyl(2-methoxy-2-phenylethyl)selane (34)

Compound **34** was synthesised following GP1 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 76 mg (41% yield). The spectral data are in agreement with literature.[16]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 – 7.33 (m, 2H), 7.32 – 7.23 (m, 7H), 7.23 – 7.17 (m, 1H), 4.20 (dd, *J* = 8.0, 5.4 Hz, 1H), 3.70 (d, *J* = 2.3 Hz, 2H), 3.22 (s, 3H), 2.90 (dd, *J* = 12.7, 8.0 Hz, 1H), 2.67 (dd, *J* = 12.7, 5.4 Hz, 1H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.3, 139.5, 129.1, 128.6, 128.5, 128.1, 126.8, 126.8, 84.3, 57.0, 31.0, 28.0 ppm

(2-Ethoxy-2-phenylethyl)(phenyl)selane (35)

Compound **35** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 157 mg (86% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 – 7.43 (m, 2H), 7.38 – 7.19 (m, 8H), 4.47 (dd, *J* = 8.5, 5.1 Hz, 1H), 3.38 (m, 3H), 3.10 (dd, *J* = 12.2, 5.1 Hz, 1H), 1.19 (t, *J* = 7.0 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.8, 132.7, 131.0, 129.1, 128.6, 128.1, 126.9, 126.7, 81.5, 64.8, 35.7, 15.4 ppm

Phenyl(2-phenyl-2-propoxyethyl)selane (36)

Compound **36** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 152 mg (79% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.30 (m, 2H), 7.28 – 7.06 (m, 8H), 4.36 (dd, *J* = 8.6, 4.9 Hz, 1H), 3.19 (m, 3H), 2.99 (dd, *J* = 12.2, 4.9 Hz, 1H), 1.58 – 1.39 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.9, 132.6, 131.2, 129.1, 128.6, 128.1, 126.8, 126.7, 81.7, 71.2, 35.9, 23.1, 10.8 ppm

IR (neat): 2958, 2874, 1477, 1091, 734, 700 cm^{-1}

(2-Butoxy-2-phenylethyl)(phenyl)selane (37)

Compound **37** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 148 mg (74% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 – 7.41 (m, 2H), 7.38 – 7.16 (m, 8H), 4.46 (dd, *J* = 8.7, 4.9 Hz, 1H), 3.40 – 3.23 (m, 3H), 3.09 (dd, *J* = 12.2, 4.9 Hz, 1H), 1.54 (m, 2H), 1.43 – 1.31 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 141.9, 132.6, 131.2, 129.1, 128.6, 128.1, 126.8, 126.7, 81.7, 69.3, 35.9, 32.0, 19.5, 14.0 ppm

(2-(Benzyloxy)-2-phenylethyl)(phenyl)selane (38)

Compound **38** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 119 mg (54% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.42 (m, 2H), 7.40 – 7.27 (m, 10H), 7.25 – 7.17 (m, 3H), 4.58 (dd, *J* = 8.4, 5.0 Hz, 1H), 4.50 (d, *J* = 11.8 Hz, 1H), 4.32 (d, *J* = 11.8 Hz, 1H), 3.45-3.83 (m, 1H), 3.12-3.18 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.2, 138.2, 132.6, 130.9, 129.1, 128.8, 128.5, 128.3, 128.0, 127.7, 126.9, 126.9, 80.9, 71.0, 35.7 ppm

(2-(But-3-yn-1-yloxy)-2-phenylethyl)(phenyl)selane (39)

Compound **39** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 112 mg (57% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 – 7.47 (m, 2H), 7.37 – 7.28 (m, 5H), 7.25 – 7.20 (m, 3H), 4.51 (dd, *J* = 8.5, 5.0 Hz, 1H), 3.52-3.42(m, 2H), 3.35 (dd, *J* = 12.4, 8.5 Hz, 1H), 3.09 (dd, *J* = 12.4, 5.0 Hz, 1H), 2.50-2.40 (m, 2H), 1.95 (t, *J* = 2.7 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.2, 132.7, 130.9, 129.1, 128.7, 128.3, 126.9, 126.8, 82.1, 81.3, 69.5, 67.4, 35.5, 20.0 ppm

IR (neat): 3057, 2868, 1477, 1437, 1095, 733, 700 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{18}H_{18}OSeNa$ [M+Na]$^+$: 349.0447, found: 349.0448

(2-(Cyclopropylmethoxy)-2-phenylethyl)(phenyl)selane (40)

Compound **40** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 150 mg (75% yield). The spectral data are in agreement with literature.[17]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44 – 7.41 (m, 2H), 7.29 – 7.13 (m, 8H), 4.44 (dd, *J* = 8.4, 5.2 Hz, 1H), 3.31 (dd, *J* = 12.2, 8.5 Hz, 1H), 3.15 – 3.07 (m, 2H), 3.04 (dd, *J* = 12.2, 5.1 Hz, 1H), 1.03 – 0.93 (m, 1H), 0.47 – 0.38 (m, 2H), 0.12 – 0.01 (m, 2H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.7, 132.6, 131.0, 129.1, 128.6, 128.1, 126.8, 126.7, 81.22, 74.0, 35.8, 10.8, 3.4, 3.1 ppm

IR (neat): 3003, 2858, 1477, 1437, 1089, 1022, 733, 700 cm^{-1}

HRMS (ESI)$^+$ calcd. for $C_{18}H_{20}OSeNa$ [M+Na]$^+$: 351.0604, found: 351.0615

(2-Isopropoxy-2-phenylethyl)(phenyl)selane (41)

Compound **41** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 134 mg (70% yield). The spectral data are in agreement with literature.[17]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 – 7.40 (m, 2H), 7.35 – 7.11 (m, 8H), 4.59 (dd, *J* = 9.9, 3.6 Hz, 1H), 3.60 – 3.44 (m, 1H), 3.31 (dd, *J* = 12.1, 8.8 Hz, 1H), 3.08 (dd, *J* = 12.1, 4.8 Hz, 1H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.08 (d, *J* = 6.2 Hz, 3H) ppm

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 132.5, 131.2, 129.1, 128.6, 128.0, 126.7, 78.9, 69.9, 36.2, 23.4, 21.5 ppm

(2-Isobutoxy-2-phenylethyl)(phenyl)selane (42)

Compound **42** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 150 mg (75% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 – 7.43 (m, 2H), 7.38 – 7.18 (m, 8H), 4.46 (dd, *J* = 8.8, 4.8 Hz, 1H), 3.36 (dd, *J* = 12.1, 8.8 Hz, 1H), 3.16 – 3.01 (m, 3H), 1.86 (m, 1H), 0.98 – 0.81 (m, 6H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 142.6, 132.4, 131.2, 129.1, 128.5, 127.9, 126.7, 78.9, 69.9, 36.2, 23.4, 21.5 ppm

(2-(Cyclopentyloxy)-2-phenylethyl)(phenyl)selane (43)

Compound **43** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 148 mg (71% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 – 7.37 (m, 2H), 7.29 – 7.10 (m, 8H), 4.47 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.92 – 3.52 (m, 1H), 3.22 (dd, *J* = 12.2, 9.2 Hz, 1H), 2.99 (dd, *J* = 12.2, 4.5 Hz, 1H), 1.74 – 1.34 (m, 8H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.5, 132.4, 131.4, 129.1, 128.6, 127.9, 126.8, 126.7, 79.6, 79.4, 36.2, 33.2, 31.7, 23.5 ppm

IR (neat): 3057, 2868, 1476, 1437, 1072, 1022, 732, 700 cm^{-1}

(2-(Cyclohexyloxy)-2-phenylethyl)(phenyl)selane (44)

Compound **44** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 135 mg (62% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (m, 2H), 7.29 – 7.09 (m, 8H), 4.57 (dd, *J* = 9.0, 4.6 Hz, 1H), 3.24 (dd, *J* = 12.1, 9.0 Hz, 1H), 3.16 – 3.07 (m, 1H), 2.99 (dd, *J* = 12.1, 4.6 Hz, 1H), 1.68 (m, 4H), 1.42 – 0.92 (m, 6H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.8, 132.3, 131.4, 129.1, 128.5, 127.9, 126.7, 126.6, 78.5, 75.7, 36.4, 33.5, 31.4, 25.9, 24.2, 24.0 ppm

IR (neat): 2927, 2854, 1477, 1436, 1070, 733, 700 cm^{-1}

(2-(*tert*-Butoxy)-2-phenylethyl)(phenyl)selane (45)

Compound **45** was synthesised following GP1 as a yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) to obtain 93 mg (47% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.31 (m, 2H), 7.27 – 7.06 (m, 8H), 4.60 (dd, *J* = 8.6, 4.8 Hz, 1H), 3.14 (dd, *J* = 12.1, 8.6 Hz, 1H), 2.95 (dd, *J* = 12.1, 4.8 Hz, 1H), 1.02 (s, 9H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 145.3, 132.2, 131.5, 129.1, 128.4, 127.4, 126.6, 126.3, 75.0, 74.2, 37.4, 28.9 ppm

IR (neat): 2972, 2931, 1477, 1436, 1072, 1190, 731, 700 cm^{-1}

1-Phenyl-2-(phenylselanyl)ethan-1-ol (46)

Compound **46** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (9:1) to obtain 134 mg (81% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 – 7.51 (m, 2H), 7.38 – 7.32 (m, 4H), 7.32 – 7.26 (m, 4H), 4.76 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.31 (dd, *J* = 12.8, 3.7 Hz, 1H), 3.15 (dd, *J* = 12.8, 9.4 Hz, 1H), 2.79 (s, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.6, 133.3, 129.4, 129.3, 128.7, 128.1, 127.6, 125.9, 72.4, 38.6 ppm

1-Phenyl-2-(phenylselanyl)ethyl formate (47)

Compound **47** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 76 mg (41% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 7.44 – 7.40 (m, 2H), 7.30 – 7.13 (m, 8H), 5.94 (dd, *J* = 8.9, 5.8 Hz, 1H), 3.32 (dd, *J* = 12.9, 8.0 Hz, 1H), 3.18 (dd, *J* = 13.2, 6.1 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 160.0, 138.8, 135.5, 133.4, 129.3, 128.8, 128.7, 127.5, 126.8, 75.1, 33.2 ppm

1-Phenyl-2-(phenylselanyl)ethyl acetate (48)

Compound **48** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 92 mg (46% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 – 7.40 (m, 2H), 7.28 – 7.16 (m, 8H), 5.87 (dd, *J* = 8.0, 5.7 Hz, 1H), 3.31 (dd, *J* = 12.8, 8.0 Hz, 1H), 3.16 (dd, *J* = 12.8, 5.7 Hz, 1H), 1.95 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.1, 139.5, 133.2, 129.9, 129.2, 128.6, 128.5, 127.3, 126.7, 75.3, 33.5, 21.2 ppm

1-(1-Phenyl-2-(phenylselanyl)ethyl)-1*H*-benzo[*d*][1,2,3]triazole (49)

Compound **49** was synthesised following GP1 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl

acetate (9:1) to obtain 147 mg (65% yield). The spectral data are in agreement with literature.[10a]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 – 7.94 (m, 1H), 7.46 – 7.39 (m, 2H), 7.38 – 7.19 (m, 11H), 5.85 (dd, *J* = 9.4, 5.8 Hz, 1H), 4.25 (dd, *J* = 13.1, 9.4 Hz, 1H), 3.82 (dd, *J* = 13.1, 5.8 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.1, 138.4, 133.7, 133.1, 129.3, 129.0, 129.0, 128.8, 127.8, 127.3, 126.9, 124.0, 120.1, 109.6, 63.6, 32.6 ppm

2-((Phenylselanyl)methyl)tetrahydrofuran (50)

Compound **50** was synthesised following GP2 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 105 mg (73% yield). The spectral data are in agreement with literature.[25]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 – 7.50 (m, 2H), 7.30 – 7.22 (m, 3H), 4.30 – 4.03 (m, 1H), 4.01 – 3.88 (m, 1H), 3.84 – 3.66 (m, 1H), 3.15 (dd, *J* = 12.2, 5.8 Hz, 1H), 3.01 (dd, *J* = 12.2, 6.9 Hz, 1H), 2.14 – 2.05 (m, 1H), 2.03 – 1.80 (m, 2H), 1.65 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.4, 132.7, 129.2, 127.0, 78.4, 78.4, 33.2, 31.7, 26.1 ppm

2-((Phenylselanyl)methyl)tetrahydro-2*H*-pyran (51)

Compound **51** was synthesised following GP2 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 103 mg (67% yield). The spectral data are in agreement with literature.[25]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 – 7.46 (m, 2H), 7.29 – 7.18 (m, 3H), 4.04 – 3.95 (m, 1H), 3.92 – 3.26 (m, 2H), 3.07 (dd, *J* = 12.2, 6.9 Hz, 1H), 2.93 (dd, *J* = 12.2, 5.7 Hz, 1H), 1.99 – 1.68 (m, 2H), 1.61 – 1.43 (m, 3H), 1.37 – 1.26 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 132.5, 130.9, 129.1, 126.8, 77.2, 68.9, 33.8, 31.9, 25.9, 23.5 ppm

2-((Phenylselanyl)methyl)tetrahydro-2*H*-pyran (52)

Compound **52** was synthesised as a 1:1 mixture (*cis* : *trans*) following GP2 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (9:1) to obtain 89 mg (58% yield). The spectral data are in agreement with literature.[21]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.61 – 7.55 (m, 4H), 7.31 – 7.23 (m, 6H), 3.96 – 3.86 (m, 3H), 3.78 (dt, *J* = 9.4, 6.6 Hz, 1H), 3.46 – 3.29 (m, 3H), 2.99 – 2.89 (m, 1H), 2.22 – 2.10 (m, 1H), 2.09 – 1.99 (m, 1H), 1.95 – 1.83 (m, 2H), 1.75 – 1.53 (m, 4H), 1.44 (d, *J* = 7.0 Hz, 3H), 1.35 (d, *J* = 6.1 Hz, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 135.6, 135.3, 134.9, 129.1, 129.0, 128.2, 127.9, 127.6, 83.0, 78.4, 68.6, 68.2, 47.2, 44.4, 32.5, 30.4, 28.2, 26.3, 21.3, 18.9 ppm

5-((Phenylselanyl)methyl)dihydrofuran-2(3*H*)-one (53)

Compound **53** was synthesised following GP2 as a pale yellow oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 101 mg (65% yield). The spectral data are in agreement with literature.[20]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62 – 7.46 (m, 2H), 7.33 – 7.26 (m, 3H), 4.69 – 4.61 (m, 1H), 3.29 (dd, *J* = 12.9, 4.8 Hz, 1H), 3.01 (dd, *J* = 12.9, 8.0 Hz, 1H), 2.62 – 2.36 (m, 3H), 2.00 – 1.90 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.7, 133.4, 129.5, 128.9, 127.8, 79.5, 32.0, 28.9, 27.8 ppm

5-Phenyl-4-(phenylselanyl)dihydrofuran-2(3*H*)-one (54)

Compound **54** was synthesised following GP2 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 58 mg (30% yield). The spectral data are in agreement with literature.[23]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 – 7.52 (m, 2H), 7.40 – 7.28 (m, 8H), 5.38 (d, *J* = 6.9 Hz, 1H), 3.79– 3.71 (m, 1H), 3.04 (dd, *J* = 18.0, 8.3 Hz, 1H), 2.67 (dd, *J* = 18.0, 8.4 Hz, 1H) ppm

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.7, 137.4, 136.3, 129.7, 129.2, 129.1, 128.9, 126.1, 125.9, 86.3, 42.38, 36.1 ppm

6-(Phenylselanyl)hexahydro-2*H*-cyclopenta[*b*]furan-2-one (55)

Compound **55** was synthesised following GP2 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 115 mg (68% yield). The spectral data are in agreement with literature.[24]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 – 7.42 (m, 2H), 7.34 – 7.25 (m, 3H), 4.90 (d, *J* = 6.3 Hz, 1H), 3.97 – 3.78 (m, 1H), 3.15 – 3.04 (m, 1H), 2.87 – 2.73 (m, 1H), 2.34 (dd, *J* = 18.4, 2.5 Hz, 1H), 2.28 – 2.18 (m, 2H), 1.91 – 1.71 (m, 1H), 1.61 – 1.51 (m, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 177.0, 133.8, 129.5, 128.8, 127.9, 90.7, 46.4, 37.2, 36.1, 32.6, 30.2 ppm

3-((Phenylselanyl)methyl)isobenzofuran-1(3*H*)-one (56)

Compound **56** was synthesised following GP2 as a colourless oil. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 87 mg (48% yield). The spectral data are in agreement with literature.[25]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97 – 7.87 (m, 1H), 7.60 – 7.45 (m, 5H), 7.30 – 7.19 (m, 3H), 5.72 – 5.55 (m, 1H), 3.46 (dd, *J* = 13.2, 5.0 Hz, 1H), 3.32 (dd, *J* = 13.2, 6.4 Hz, 1H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 169.9, 148.5, 133.8, 133.6, 129.5, 129.2, 129.0, 127.7, 126.6, 125.7, 122.4, 79.1, 31.8 ppm

2-((Phenylselanyl) methyl)-1-tosylindoline (57)

Compound **57** was synthesised following GP2 as a yellow solid. It was purified by column chromatography on silica gel using hexane/ethyl acetate (4:1) to obtain 87 mg (33% yield). The spectral data are in agreement with literature.[26]

m.p. = 70 – 72 ºC

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.1 Hz, 1H), 7.61 – 7.54 (m, 2H), 7.39 – 7.29 (m, 5H), 7.23 – 7.18 (m, 1H), 7.11 – 7.08 (m, 2H), 7.04 – 7.01 (m, 2H), 4.36 – 4.11 (m, 1H), 3.65 (dd, *J* = 12.5, 3.5 Hz, 1H), 2.96 – 2.81 (m, 3H), 2.32 (s, 3H) ppm

^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.0, 141.4, 134.7, 132.6, 131.1, 129.7, 129.4, 128.9, 127.9, 127.2, 127.1, 125.3, 124.8, 117.1, 61.7, 34.2, 33.2, 21.6 ppm

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Supporting Information

Yes

Primary Data

No

References

(1) (a) Alcácer, V.; Cruz-Machado, V. *Eng. Sci. Technol. Int. J.* **2019**, *22*, 899. (b) Fitzpatrick, D. E.; Battilocchio, C.; Ley S. V. *ACS Cent. Sci.* **2016**, *2*, 131. (c) Kreimeyer, A.; Eckes, P.; Fischer, C.; Lauke, H.; Schuhmacher, P. *Angew. Chem. Int. Ed.* **2015**, *54*, 3178. (d). Ley, S. V; Fitzpatrick, D. E.; Myers, R. M.; Battilocchio, C.; Ingham, R. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 10122. (e) Prieto, G.; Schüth, F. *Angew. Chem.*

Int. Ed. **2015**, *54*, 3222. (f) Ley, S. V.; Fitzpatrick, D. E.; Ingham, R. J.; Myers, R. M. *Angew. Chem. Int. Ed.* **2015**, *54*, 3449.

(2) (a) *Science of Synthesis: Flow Chemistry*; Jamison, T. F.; Koch, G. Eds., Thieme: Stuttgart **2018**. (b) *Microreactors in Organic Synthesis and Catalysis*; Wirth, T. Ed., Wiley-VCH: Weinheim, **2013**. (c) Yoshida, J. *Flash Chemistry: Fast Organic Synthesis in Microsystems*, Wiley-VCH: Weinheim, **2008**.

(3) (a) Jing, Q; Moeller, K. D. *Acc. Chem. Res.* **2020**, *53*, 135. (b) Folgueiras Amador A. A.; Wirth T. in *Science of Synthesis: Flow Chemistry*; Jamison, T. F.; Koch, G. Eds., Thieme: Stuttgart **2018**, 147. (c) Pletcher, D.; Green, R. A.; Brown, R. C. D. *Chem. Rev.* **2018**, *118*, 4573. (d) Atobe, M.; Tateno, H.; Matsumura, Y. *Chem. Rev.* **2018**, *118*, 4541. (e) Wiebe, A.; Gieshoff, T.; Möhle, S.; Rodrigo, E.; Zirbes, M.; Waldvogel, S. R. *Angew. Chem. Int. Ed.* **2018**, *57*, 5594.

(4) (a) Elsherbini, M.; Wirth, T. *Acc. Chem. Res.* **2019**, *52*, 3287. (b) Folgueiras-Amador A. A.; Philipps, K.; Guilbaud, S.; Poelakker, J.; Wirth, T. *Angew. Chem. Int. Ed.* **2017**, *56*, 15446.

(5) https://www.vapourtec.com/products/flow-reactors/ion-electrochemical-reactor-features/, accessed January 2020.

(6) (a) Shaabani, S.; Xu, R.; Ahmadianmoghaddam, M.; Gao, L.; Stahorsky, M. Olechno, J.; Ellson, R.; Kossenjans, M.; Helan, V.; Dömling, A. *Green Chem.* **2019**, *21*, 225. (b) Trobe, M.; Burke, M. D. *Angew. Chem. Int. Ed.* **2018**, *57*, 4192. (c) Panza, M.; Pistorio, S. G.; Stine, K. J.; Demchenko, A. V. *Chem. Rev.* **2018**, *118*, 8105. (d) Mijalis, A. J.; Thomas, D. A.; Simon, M. D.; Adamo, A.; Beaumont, R.; Jensen, K. F.; Pentelute, B. L. *Nat. Chem. Biol.* **2017**, *13*, 464. (e) Reizman, B. J.; Jensen, K. F. *Acc. Chem. Res.* **2016**, *49*, 1786. (f) Yoshida, J.; Kim, H.; Nagaki, A. *ChemSusChem* **2011**, *4*, 331. (g) Merrifield, R. B.; Stewart, J. M.; Jernberg, N. *Anal. Chem.* **1966**, *38*, 1905.

(7) (a) Singh, F. V.; Wirth, T. *Catal. Sci. Technol.* **2019**, *9*, 1073. (b) Singh, F. V.; Wirth, T. in *Organoselenium Compounds in Biology and Medicine: Synthesis, Biological and Therapeutic Treatments,* Eds. Jain, V. K.; Priyadarsini, K. I. The Royal Society of Chemistry, **2018**, 77. (c) Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. *Chem. Rev.* **2010**, *110*, 4357. (d) Wirth, T. Ed., *Organoselenium Chemistry*, Springer, Berlin, Heidelberg, **2000**. (e) Back, T. G. *Organoselenium Chemistry: A Practical Approach*, New York: Oxford University Press, **1999**.

(8) Niyomura, O.; Cox, M.; Wirth, T. *Synlett* **2006**, 251.

(9) (a) Jiang, Y.; Xu, K.; Zeng, C. *Chem. Rev.* **2018**, *118*, 4485. (b) Moeller, K. D. *Chem. Rev.* **2018**, *118*, 4817. (c) Francke, R.; Schille, B.; Roemelt, M. *Chem. Rev.* **2018**, *118*, 4631. (d) Yoshida, J.; Shimizu, A.; Hayashi, R. *Chem. Rev.* **2018**, *118*, 4702. (e) Ibanez, J. G.; Rincón, M. E.; Gutierrez-Granados, S.; Chahma, M.; Jaramillo-Quintero, O. A.; Frontana-Uribe, B. A. *Chem. Rev.* **2018**, *118*, 4731. (f) Nutting, J. E.; Rafiee, M.; Stahl, S. S. *Chem. Rev.* **2018**, *118*, 4834.

(10) (a) Yuan, Y.; Lei, A. *Acc. Chem. Res*. **2019**, *52*, 3309. (b) Sun, L.; Yuan, Y.; Yao, M.; Wang, H.; Wang, D.; Gao, M.; Chen, Y. H.; Lei, A. *Org. Lett.* **2019**, *21*, 1297. (c) Chen, J.; Mei, L.; Wang, H.; Hu, L.; Sun X.; Shi, J.; Li.; Q. *ChemistryOpen* **2019**, *7*, 1230. (d) Wilken, M.; Ortgies, S.; Breder, A.; Siewert, I. *ACS Catal.* **2018**, *8*, 10901.

(11) (a) Folgueiras-Amador, A. A.; Qian, X.-Y.; Xu, H.-C.; Wirth, T. *Chem. Eur. J.* **2018**, *24*, 487. (b) Laudadio, G.; Straathof, N. J. W.; Lanting, M. D.; Knoops, B.; Hessel, V.; Noël, T. *Green Chem.* **2017**, *19*, 4061.

(12) Kaye, A.; Neidle, S.; Reese, C. B. *Tetrahedron Lett.* **1988**, *29*, 2711.

(13) Meirinho, A. G.; Pereira, V. F.; Martins, G. M.; Saba, S.; Rafique, J.; Braga, A. L.; Mendes, S. R. *Eur. J. Org. Chem.* **2019**, 6465.

(14) CCDC-1980248 (**21**) 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/data_request/cif.

(15) Perin, G.; Santoni, P.; Barcellos, A. M.; Nobre, P. C.; Jacob, R. G.; Lenardão, E. J.; Santi, C. *Eur. J. Org. Chem.* **2018**, 1224.

(16) Yu, C.; Shi, H.; Yan, J. *Arkivoc* **2015**, 266.

(17) Vieira, A. A.; Azeredo, J. B.; Godoi, M.; Santi, C.; Da Silva Júnior, E. N.;. Braga, A. L *J. Org. Chem*. **2015**, *80*, 2120.

(18) Bosman, C.; D'Annibale, A.; Resta, S.; Trogolo, C. *Tetrahedron Lett.* **1994**, *35*, 6525.

(19) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* **1988**, *44*, 2261.

(20) Conner, E. S.; Crocker, K. E.; Fernando, R. G.; Fronczek, F. R.; Stanley, G. G.; Ragains, J. R. *Org. Lett.* **2013**, *15*, 5558.

(21) Kostić, M.; Verdía, P.; Fernández-Stefanuto, V.; Puchta, R.; Tojo, E. *J. Phys. Org. Chem.* **2019**, *32*, 1.

(22) Vásquez-Céspedes, S.; Ferry, A.; Candish, L.; Glorius, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 5772.

(23) Denmark, S. E.; Collins, W. R. *Org. Lett.* **2007**, *9*, 3801.

(24) Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 3884.

(25) Zhang, Q. B.; Yuan, P. F.; Kai, L. L.; Liu, K.; Ban, Y. L.; Wang, X. Y.; Wu, L. Z.; Liu, Q. *Org. Lett.* **2019**, *21*, 885.

(26) Ni, Y.; Zuo, H.; Li, Y.; Wu, Y.; Zhong, F. *Org. Lett.* **2018**, *20*, 4350.