Automated Electrochemical Selenenylation

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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 selenylated products have been synthesised in short reaction time with good to high yields.

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

There has been large efforts in developing technologies in organic synthesis to enhance product output in shorter time. Continuous flow syntheses and electrochemical reactions 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. A much improved device is now commercially available. 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.

Organoselenium compounds are interesting molecules owing to their importance in medicinal chemistry, material chemistry and as reagents and catalysts. We have investigated many different aspects of selenium chemistry in the past including some batch electrochemical transformations. 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. The synthesis of β-substituted selenides electrochemically is a very promising approach as shown also in recent publications. 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.

As a model reaction, styrene (0.15 M), diphenyl diselenide (0.05 M) and CH₂OH (30 equiv) in CH₂CN 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 tetraethylammonium tetrafluoroborate (Bu₄NBF₄) 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 20 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 tetraethylammonium tetrafluoroborate (Bu₄NBF₄) as a supporting electrolyte. We discovered that under flow conditions only catalytic amounts of Bu₄NBF₄ 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.

Also different electrode materials were screened⁴ (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 Isola 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 1. Selenenylation of alkenes.](image)

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 substituted alkenes did not lead to any product formation. Allyl-substituted alkenes lead, as known, to regioisomeric mixtures (28 – 30). While 3,4-dihydro-2H-pyran formed product 24 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$_3$CN 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. Benzo[1,3]dithiazole as an N-nucleophile participated in this reaction to form the aminoselenenylation 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, dibhydroindole 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. 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. The oxidation potential required for a subsequent elimination of the selenide is not reached here.

Figure 2. Electrochemical selenenylation.

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 selenenylation 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 alkyl and aza-selenenylation 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® Isola Easy 404 using Biotage® cartridges SNAP Ultra 10 g. ¹H NMR, ¹³C NMR and ³¹P NMR spectra were measured on Bruker DPX 400 or 500 apparatus and were referenced to the residual proton solvent peak (¹H: CDCl$_3$, 7.27 ppm; DMSO-d$_6$, 2.50 ppm) and solvent ¹³C signal (CDCl$_3$, 77.2 ppm, DMSO-d$_6$, 39.35). Chemical shifts δ were reported in ppm, multiplicity of the signals was declared as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sex = sextet, hop = 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 Waters LCR Premier High Resolution Mass Spectrometer in a positive mode using Electrospray Ionisation (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 powered by an Ion electrochemical power supply. The cyclic voltammograms (SI) were performed using an Orion galv 5000 Potentiostat / Galvanostat with OGPfwr power supply.

General procedure for electrochemical oxyselenenylation 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$_2$CN) placed in vial A and mixture of diphenyl diselenide (0.05 M), alcohol (30 equiv) and TBAI (0.0075 M) in CH$_2$CN was placed in vial B. Each solution was injected into an 8 mL sample loop. After that, the reactor temperature was set at 25 ℃ with the flow rate 0.6 mL/min and the current was set at 192 mA turn on. Automated flow technology was performed using Biotage® Isola Easy 404 using Biotage® cartridges SNAP Ultra 10 g. ¹H NMR, ¹³C NMR and ³¹P NMR spectra were measured on Bruker DPX 400 or 500 apparatus and were referenced to the residual proton solvent peak (¹H: CDCl$_3$, 7.27 ppm; DMSO-d$_6$, 2.50 ppm) and solvent ¹³C signal (CDCl$_3$, 77.2 ppm, DMSO-d$_6$, 39.35). Chemical shifts δ were reported in ppm, multiplicity of the signals was declared as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sex = sextet, hop = 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 Waters LCR Premier High Resolution Mass Spectrometer in a positive mode using Electrospray Ionisation (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 powered by an Ion electrochemical power supply. The cyclic voltammograms (SI) were performed using an Orion galv 5000 Potentiostat / Galvanostat with OGPfwr power supply.

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General procedure for electrochemical selenenylation (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$_2$CN) placed in vial A and mixture of diphenyl diselenide (0.05 M) and TBAI (0.0075 M) in CH$_2$CN was placed in vial B. Each solution was injected to 8 mL sample loop. After that, the reactor temperature was set at 25 ℃ with the flow rate 0.6 mL/min and the current set at 192 mA turn on.
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 reactor. After reaching a steady state, the solution (12 mL) was collected automatically into a collection glass vessel. 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.

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta = 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

\[ \text{C NMR (101 MHz, CDCl}_3\): } \delta = 139.5, 133.9, 132.8, 130.5, 129.2, 128.9, 127.1, 127.1, 127.0, 125.0, 82.7, 57.2, 53.5 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.

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta = 7.70 – 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

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta = 141.2, 140.9, 140.0, 132.8, 130.8, 129.1, 128.9, 127.4, 127.4, 127.2, 126.9, 83.1, 57.2, 53.5 ppm

IR (neat): 2981, 2820, 1477, 1437, 1085, 732, 692 cm\(^{-1}\)

HRMS (ESI\(^+\)) calc. for C\(_{20}\)H\(_{17}\)BrSe\(_{1}\): m/z 333.0522, found: 333.0525

(2-Methoxy-2-(4-tolyloxy)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 184 mg (83% yield).

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta = 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

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta = 141.0, 138.4, 132.7, 130.9, 129.1, 129.0, 128.6, 127.4, 126.9, 125.8, 83.4, 57.2, 53.5 ppm

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

HRMS (ESI\(^+\)) calc. for C\(_{22}\)H\(_{22}\)Se\(_{1}\): m/z 371.0766, found: 371.0746

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

Compound 13 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 114 mg (61% yield).

\[ \text{H NMR (500 MHz, CDCl}_3\): } \delta = 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

\[ \text{C NMR (126 MHz, CDCl}_3\): } \delta = 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 = 25.6 Hz), 113.5, 82.0 (d, J = 2.5 Hz), 57.3, 53.5 ppm

\[ \text{IR (neat): 2972, 2822, 1477, 1436, 1089, 1072, 733 cm}^{-1}\]

HRMS (ESI\(^+\)) calc. for C\(_{15}\)H\(_{13}\)Se\(_{1}\): m/z 271.0366, found: 271.0374
HRMS (ESI)\textsuperscript{+} calc. for C\textsubscript{15}H\textsubscript{12}SeCl\textsubscript{2}M–OMe\textsuperscript{−}: 290.9820, found: 290.9810

(2-(3-Bromophenyl)-2-methoxyethyl)phenylselane (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).

\[
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3): \delta = 7.48 – 7.40 (m, 4H), 7.26 – 7.18 (m, 5H), 4.30 (dd, J = 8.1, 5.3 Hz, 1H), 3.28 (dd, J = 12.4, 8.1 Hz, 1H), 3.25 (s, 3H), 3.06 (dd, J = 12.4, 5.3 Hz, 1H) ppm
\]

\[
\text{\textsuperscript{13}C NMR (126 MHz, CDCl}_3): \delta = 143.5, 132.9, 131.3, 130.4, 1303, 129.9, 129.2, 127.2, 127.2, 125.5, 122.9, 82.8, 57.4, 35.2 ppm}
\]

HRMS (ESI)\textsuperscript{+} calc. for C\textsubscript{16}H\textsubscript{14}BrSe[M–OMe]\textsuperscript{−}: 334.9315, found: 334.9301

(2-Methoxy-2-phenylpropyl)ph edadicyl 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.\textsuperscript{17}

\[
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3): \delta = 7.43 – 7.39 (m, 4H), 7.36 – 7.32 (m, 2H), 7.29 – 7.25 (m, 1H), 7.20 – 7.16 (m, 3H), 3.43 (d, J = 11.3 Hz, 1H), 3.28 (d, J = 11.8 Hz, 1H), 3.13 (s, 3H), 1.72 (s, 3H) ppm}
\]

\[
\text{\textsuperscript{13}C NMR (126 MHz, CDCl}_3): \delta = 143.8, 132.8, 131.5, 129.0, 128.4, 127.5, 126.8, 126.4, 79.1, 51.2, 42.6, 23.3 ppm}
\]

(2-Methoxy-3-methyl-2-phenylbutyl)ph edadicyl 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).

\[
m.p. = 87 – 88 °C
\]

\[
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3): \delta = 7.60 – 7.55 (m, 2H), 7.36 – 7.24 (m, 4H), 3.79 (d, J = 12.0 Hz, 1H), 3.62 (d, J = 12.0 Hz, 1H), 3.26 (s, 3H), 2.41 (dt, J = 13.6, 6.8 Hz, 1H), 0.79 (d, J = 6.7 Hz, 3H), 0.75 (d, J = 6.9 Hz, 3H) ppm}
\]

\[
\text{\textsuperscript{13}C NMR (126 MHz, CDCl}_3): \delta = 139.3, 133.3, 131.0, 129.0, 128.0, 127.6, 127.1, 127.1, 127.0, 82.2, 50.9, 35.4, 34.8, 18.2, 16.9 ppm}
\]

HRMS (ESI)\textsuperscript{+} calc. for C\textsubscript{15}H\textsubscript{14}BrSeM–OMe\textsuperscript{−}: 334.9315, found: 334.9301

(2-Methoxy-2-diphenylethyl)ph edadicyl 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.\textsuperscript{18}

\[
m.p. = 76 – 78 °C
\]

\[
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_3): \delta = 7.45 – 7.38 (m, 4H), 7.33 – 7.28 (m, 4H), 7.26 – 7.17 (m, 5H), 3.96 (s, 2H), 3.16 (s, 3H) ppm}
\]

\[
\text{\textsuperscript{13}C NMR (126 MHz, CDCl}_3): \delta = 144.3, 133.3, 130.9, 129.0, 128.1, 127.3, 127.1, 127.0, 82.2, 50.9, 37.9 ppm}
\]

(1-Methoxy-1-phenylpropan-2-yl)ph edadicyl 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.\textsuperscript{19}

\[
m.p. = 82 – 83 °C
\]

\[
\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3): \delta = 7.61 – 7.54 (m, 4H), 7.38 – 7.22 (m, 4H), 4.41 (d, J = 4.5 Hz, 1H), 3.48 (qd, J = 7.0, 4.5 Hz, 1H), 3.30 (s, 3H), 1.35 (d, J = 7.1 Hz, 3H) ppm}
\]

\[
\text{\textsuperscript{13}C NMR (101 MHz, CDCl}_3): \delta = 139.8, 134.7, 130.1, 129.3, 128.4, 127.9, 127.5, 127.2, 86.5, 57.7, 45.9, 16.5 ppm}
\]

(2-Methoxy-2-(naphthalen-2-yl)ethyl)ph edadicyl selane (26)

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

\[
\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3): \delta = 7.87 – 7.81 (m, 3H), 7.75 (s, 1H), 7.52 – 7.42 (m, 5H), 7.25 – 7.14 (m, 4H), 4.52 (dd, J = 8.3, 5.2 Hz, 1H), 3.40 (dd, J = 12.3, 4.0 Hz, 1H), 3.29 (s, 3H), 3.19 (dd, J = 12.3, 5.2 Hz, 1H) ppm}
\]

\[
\text{\textsuperscript{13}C NMR (126 MHz, CDCl}_3): \delta = 138.5, 134.4, 133.5, 133.4, 132.9, 130.8, 129.2, 128.8, 128.2, 127.9, 127.1, 126.5, 126.4, 126.3, 124.3, 83.6, 77.3, 53.7, 35.4 ppm}
\]

HRMS (ESI)\textsuperscript{+} calc. for C\textsubscript{21}H\textsubscript{18}SeM–OMe\textsuperscript{−}: 307.0366, found: 307.0359

(1-Methoxy-2,3-dihydro-1H-inden-2-yl)ph edadicyl selane (27)

Compound 27 was synthesised following GP1 as an 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.\textsuperscript{16}
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

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

Compounds 29a and 29b 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 43% isolated yield (76 mg). The spectral data are in agreement with literature.16

\[ \text{IR (neat): 2974, 2920, 2850, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 249.0522, found: 249.0524.

\[ \text{(2-Cyclopentyl-2-methoxyethyl)(phenyl)selane (28a) and (1-Cyclopentyl-2-methoxyethyl)(phenyl)selane (28b)} \]

Compound 29 was synthesised following the GP1 as a 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).

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

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).

\[ \text{IR (neat): 2974, 2920, 2850, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 263.0685, found: 263.0685.

\[ \text{(2-Methoxycthyl)(phenyl)selane (30a) and (1-Methoxyctyl-2-yl)(phenyl)selane (30b)} \]

Compounds 30a and 30b were 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.15

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

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.15

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

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

\[ \text{IR (neat): 2974, 2920, 2850, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

Compounds 33a and 33b 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 125 mg (72% yield). The spectral data are in agreement with literature.22

\[ \text{IR (neat): 2974, 2920, 2850, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 249.0522, found: 249.0524.

\[ \text{(2-Methoxycthyl)(phenyl)selane (30a) and (1-Methoxyctyl-2-yl)(phenyl)selane (30b)} \]

Compounds 30a and 30b were 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 157 mg (86% yield). The spectral data are in agreement with literature.15

\[ \text{IR (neat): 2947, 2866, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 263.0685, found: 263.0685.

\[ \text{(2-Methoxyctyl)(phenyl)selane (30a) and (1-Methoxyctyl-2-yl)(phenyl)selane (30b)} \]

Compounds 30a and 30b were 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 130 mg (80% yield). The spectral data are in agreement with literature.15

\[ \text{IR (neat): 2947, 2866, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

Compound 33 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.23

\[ \text{IR (neat): 2974, 2920, 2850, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 249.0522, found: 249.0524.

\[ \text{(2-Methoxycthyl)(phenyl)selane (30a) and (1-Methoxyctyl-2-yl)(phenyl)selane (30b)} \]

Compounds 30a and 30b were 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 148 mg (74% yield). The spectral data are in agreement with literature.23

\[ \text{IR (neat): 2947, 2866, 1577, 1475, 1403, 1095, 906, 729, 609 cm}^{-1} \]

HRMS (ESI)\(^+\) calcld for C\(_{12}\)H\(_{13}\)O\(_3\)Si: 249.0522, found: 249.0524.

\[ \text{(2-Methoxycthyl)(phenyl)selane (30a) and (1-Methoxyctyl-2-yl)(phenyl)selane (30b)} \]
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.16

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

HRMS (ESI): calcd. for \( \text{CH}_{28}\text{OSi} \): 349.0447, found: 349.0448

\[ \text{(2-Morpholino-2-phenylethyl)(phenyl)selane (40)} \]

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

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

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{30}\text{O} \text{SeNa} \): 351.0604, found: 351.0615

\[ \text{(2-Iso-propoxy-2-phenylethyl)(phenyl)selane (41)} \]

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

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{24}\text{H}_{34} \text{OSeNa} \): 351.0604, found: 351.0615

\[ \text{(2-Isobutoxy-2-phenylethyl)(phenyl)selane (42)} \]

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.17

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{24}\text{H}_{34} \text{OSeNa} \): 351.0604, found: 351.0615

\[ \text{(2-Cyclopentenyl)-2-phenylethyl)(phenyl)selane (43)} \]

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). The spectral data are in agreement with literature.16

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

HRMS (ESI): calcd. for \( \text{C}_{26}\text{H}_{36} \text{OSeNa} \): 351.0604, found: 351.0615

\[ \text{(2-Phenyl-2-(phenylethyl)selanyl)ethanol (46)} \]

Compound 46 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). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{28} \text{O} \text{SeNa} \): 349.0447, found: 349.0448

\[ \text{(2-Piperidino-2-phenylethyl)(phenyl)selane (47)} \]

Compound 47 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 76 mg (41% yield). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{24}\text{H}_{34} \text{OSeNa} \): 351.0604, found: 351.0615

\[ \text{(1-Phenyl-2-(phenylethyl)ethan-1-ol (48)} \]

Compound 48 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 93 mg (47% yield). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{28} \text{O} \text{SeNa} \): 349.0447, found: 349.0448

\[ \text{1-Phenyl-2-(phenylethyl)ethan-1-ol (49)} \]

Compound 49 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 135 mg (62% yield). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{28} \text{O} \text{SeNa} \): 349.0447, found: 349.0448

\[ \text{(2-Cyclohexyl-2-phenylethyl)(phenyl)selane (50)} \]

Compound 50 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

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{28} \text{O} \text{SeNa} \): 349.0447, found: 349.0448

\[ \text{(2-(Cyclohexylmethoxy)-2-phenylethyl)(phenyl)selane (52)} \]

Compound 52 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). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]

HRMS (ESI): calcd. for \( \text{C}_{22}\text{H}_{28} \text{O} \text{SeNa} \): 349.0447, found: 349.0448

\[ \text{(2-Cyclohexyloxy-2-phenylethyl)(phenyl)selane (53)} \]

Compound 53 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). The spectral data are in agreement with literature.13

\[ \text{IR (neat): 3017, 2837, 1477, 1437, 1095, 733, 700 cm}^{-1} \]
acetate (9:1) to obtain 147 mg (65% yield). The spectral data are in agreement with literature.12

\[ \text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 8.10 - 7.94 (\text{m, 1H}), 7.46 - 7.39 (\text{m, 2H}), 7.38 - 7.19 (\text{m, 11H}), 5.85 (dd, } J = 9.4, 5.8 \text{ Hz, 1H), 4.25 (dd, } J = 13.1, 9.4 \text{ Hz, 1H), 3.82 (dd, } J = 13.1, 5.8 \text{ Hz, 1H} \text{ ppm.} \]

\[ \text{C NMR (126 MHz, CDCl}_3\text{): } \delta = 146.1, 138.4, 133.7, 133.1, 129.3, 129.0, 129.8, 127.8, 127.3, 126.9, 124.0, 120.1, 109.6, 63.6, 32.6 \text{ ppm.} \]

2-(Phenylselanyl)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 101 mg (65% yield). The spectral data are in agreement with literature.20

\[ \text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 7.62 - 7.46 (\text{m, 2H}), 7.33 - 7.26 (\text{m, 3H}), 4.69 - 4.61 (\text{m, 1H}), 3.29 (dd, } J = 12.9, 4.8 \text{ Hz, 1H), 3.01 (dd, } J = 12.9, 8.0 \text{ Hz, 1H), 2.62 - 2.36 (m, 3H), 2.00 - 1.90 (m, 1H) \text{ ppm.} \]

\[ \text{C NMR (126 MHz, CDCl}_3\text{): } \delta = 176.7, 133.4, 129.5, 128.9, 127.8, 79.5, 32.0, 28.9, 27.8 \text{ ppm.} \]

5-Phenyl-4-(phenylselanyl)dihydrofuran-2(3H)-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.21

\[ \text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 7.55 - 7.52 (\text{m, 2H}), 7.40 - 7.28 (\text{m, 8H}), 5.38 (d, } J = 6.9 \text{ Hz, 1H), 3.79 - 3.71 (\text{m, 1H}), 3.04 (dd, } J = 18.0, 8.3 \text{ Hz, 1H), 2.67 (dd, } J = 18.0, 8.4 \text{ Hz, 1H) ppm.} \]

\[ \text{C NMR (101 MHz, CDCl}_3\text{): } \delta = 174.7, 137.4, 136.3, 129.7, 129.2, 129.1, 128.9, 126.1, 125.9, 86.3, 42.88, 36.1 \text{ ppm.} \]

Acknowledgment

We thank D. Guthrie and M. Nuno, Vapourtec Inc., for many discussions and for providing the equipment and support for this research. Fruitful discussions with Dr. M. N. Khan, Cardinal University, are gratefully acknowledged. Support from Cardinal University and from the Chemistry Department, Jazan University, Saudi Arabia, are appreciated.

Supporting Information

Yes

Primary Data

No

References


(14) CCC-1988248 (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.


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


