Article:
Cooksey, JP, Kocieński, PJ and Blacker, AJ orcid.org/0000-0003-4898-2712 (2019) A Scalable Process for the Synthesis of 1,2-Dialkyldiselanes and 1-Alkaneselenols. Organic Process Research & Development, 23 (11). pp. 2571-2575. ISSN 1083-6160

https://doi.org/10.1021/acs.oprd.9b00380

A Scalable Process for the Synthesis of 1,2-Dialkyldiselanes and 1-Alkaneselenols

John P. Cooksey,[†] Philip J. Kocieński,[†] A. John Blacker[†‡]*

Institute of Process Research and Development: [†] School of Chemistry, University of Leeds, Leeds; [‡] School of Chemical and Process Engineering, University of Leeds, LS2 9JT, UK

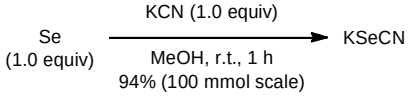
SUPPORTING INFORMATION

1. General Information and Materials

All reagents and solvents obtained from commercial suppliers and were used as supplied unless stated otherwise. All reactions were magnetically stirred under an atmosphere of nitrogen unless stated otherwise and monitored by thin layer chromatography (TLC) using 0.25 mm E. Merck pre-coated silica gel plates visualised with UV light followed by 20% w/v phosphomolybdic acid in ethanol. Organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo using a rotary evaporator. All yields refer to products judged to be ≥95% pure by ^{1}H and ^{13}C NMR spectroscopy unless stated otherwise. NMR spectra were recorded on Bruker DPX-300 and DRX-500 Fourier transform spectrometers using an internal deuterium lock in the solvents specified. Chemical shifts (δ) are reported in ppm relative to the residual signals of chloroform ($\delta_H = 7.26$, $\delta_C = 77.2$) and DMSO ($\delta_H = 2.50$, $\delta_C = 39.5$). Coupling constants (J) are reported in Hertz (Hz) with multiplicities described using the following abbreviations: app = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, oct = octet and m = multiplet. In ^{13}C NMR spectra, multiplicities and signal assignments were elucidated using DEPT 135 experiments. Infrared spectra were recorded on a Bruker FT-IR spectrometer fitted with a diamond transmission accessory; details are reported as ν_{max} in cm^{-1}, followed by a peak intensity descriptor using the following abbreviations: s = strong, m = medium, w = weak, br = broad. Mass spectrometry was carried out using a Micromass LCT (ES mode) or Bruker Daltonic (ES mode) spectrometer. Melting points were measured using a Griffin melting point apparatus and are uncorrected. All reactions and purifications were conducted in a well ventilated fume hood with adequate protection. Aqueous solutions of potassium cyanide were destroyed with bleach as described below.

2. Experimental procedures

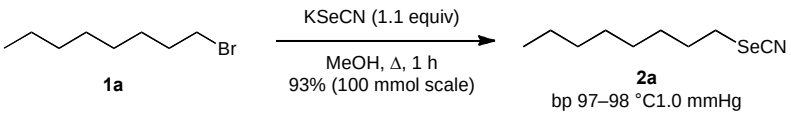
2.1 Synthesis of potassium selenocyanate (KSeCN)



To a magnetically stirred suspension of selenium powder (100 mesh, 7.9 g, 100 mmol, 1.0 equiv) in methanol (100 mL) was added at room temperature potassium cyanide (6.5 g, 100 mmol, 1.0 equiv) in a single portion. Within a few minutes a mild exothermic reaction ensued raising the internal temperature to 35 °C. As the reaction proceeded, the selenium dissolved leaving a turbid, light grey reaction mixture. After stirring at ambient temperature for 1 h, the reaction mixture was filtered through a 1 cm pad of celite and then concentrated in vacuo to an off-white solid. The crude potassium selenocyanate was slurried in hot 2-propanol and then allowed to cool to room temperature. The resultant 2-propanol solvate of potassium selenocyanate was collected by suction filtration and washed with 2-propanol. The labile solvate lost 2-propanol on storage at 1.0 mmHg for 16 h at room temperature to give potassium selenocyanate (13.5 g, 93.6 mmol, 94%) as a white solid.

2.2 Synthesis of 1-octaneselenol with isolation and purification of two intermediates (4a).

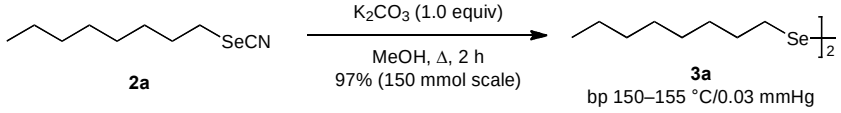
2.2.1 1-octaneselenocyanate (2a).



1-Bromooctane (100 mmol, 1.0 equiv) was added as a single portion to a magnetically stirred solution of potassium selenocyanate (15.84 g, 110 mmol, 1.1 equiv) in methanol (75 mL) at room temperature. The reaction mixture was stirred at reflux for 1 h during which time a white precipitate of potassium bromide formed. After cooling to room temperature, the reaction mixture was poured into ice water (300 mL) and the pale yellow oil extracted into hexanes (2 × 300 mL). The combined organic extracts (STENCH) were dried (Na_2SO_4) and concentrated in vacuo at ca. 10 °C. The residual yellow oil was purified by short path distillation. In order to remove malodorous volatiles, the distillation apparatus was initially fitted with a dry ice–acetone cooled collector and a vacuum (ca 20 mmHg) applied. The pot temperature was increased to ca. 60 °C whereupon a pale yellow distillate (ca 4.0 mL) was collected. After 10 min the vacuum was increased to ca. 1.0 mmHg in order to remove any remaining volatiles. After fitting a fresh collector, the pot temperature was gradually increased and the 1-octane1selenocyanate (**2a**, 20.3 g, 93 mmol, 93%) isolated as a pale yellow oil bp 97–98 °C/1.0 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.05 (2H, t, J = 7.4, C1H_2), 1.90 (2H, quint, J = 7.4, C2H_2), 1.48–1.38 (2H, m, CH_2), 1.38–1.22 (8H, m, 4 × CH_2), 0.88 (3H, t, J = 7.0, C8H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 101.7 (SeCN), 31.8 (CH_2), 30.9 (CH_2), 29.8 (C1H_2; $^1J_{Se–C}$ = 50.1), 29.2 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 22.7 (CH_2), 14.2 (C8H_3). IR (thin film): ν = 2150 m (CN) cm^{-1}.

The aqueous layer contains potassium cyanide (ca. 10 mmol) which was destroyed with household bleach as described below.

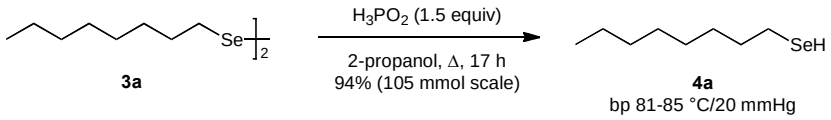
2.2.2 1,2-dioctyldiselane (3a).



A mixture of 1-octaneselenocyanate (**2a**, 32.7 g, 150 mmol) and K_2CO_3 (20.7 g, 150 mmol, 1.0 equiv) in MeOH (150 mL) was heated at reflux for 2 h. After cooling to room temperature, the mixture was poured into H_2O (450 mL). The orange oil that separates was extracted into 40–60 petrol (2 × 225 mL). The aqueous phase was saved for waste treatment as described below. The combined organic extracts were washed with H_2O (100 mL), dried (Na_2SO_4) and concentrated in vacuo. The residual orange oil was purified by short path distillation to give 1,2-dioctyldiselane (**3a**, 72.75 mmol, 97%) as an orange oil: bp 150–155 °C/0.03 mmHg; lit.[1] bp 197–205 °C/3 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.91 (4H, app t, J = 7.3, C1H_2), 1.72 (4H, app quint, J = 7.4, C2H_2), 1.42–1.34 (4H, m, 2 × CH_2), 1.34–1.22 (16H, m, 8 × CH_2), 0.88 (6H, t, J = 6.9 Hz, C8H_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.0 (2C, CH_2), 30.8 (2C, CH_2), 30.1 (2C, CH_2), 29.3 (2C, CH_2), 29.3 (2C, CH_2), 24.1 (2C, CH_2; $^1J_{Se–C}$ = 60.7), 22.8 (2C, CH_2), 14.2 (2C, CH_3). LRMS (EI$^+$ mode): m/z = 386 [M$^+$, 100%], 272 (95%), 176 (80%). HRMS (EI$^+$ mode): m/z = 386.0989 [M$^+$, 100%]; calculated for $C_{16}H_{34}Se_2$ [M$^+$]: m/z = 386.0991. ^{1}H NMR data (400 MHz) for 1,2-dioctyldiselane has been reported.[2]

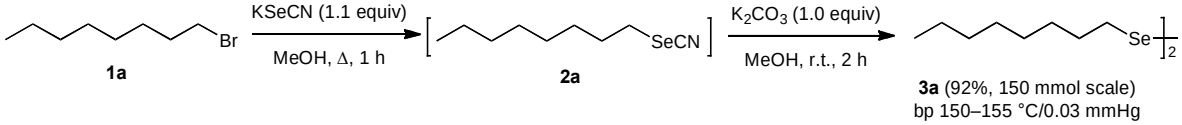
The aqueous layer contains potassium cyanide (ca. 150 mmol) which was destroyed with household bleach (5.25%, 0.74 M, 2.5 mL/mmol cyanide) according to the procedure of M.-A. Armour, J. Chem. Ed. 1988, 65, 64A. The presence of any remaining cyanide was assayed using the Prussian blue test. To one mL of the solution add 2 drops of a freshly prepared 5% aqueous solution of ferrous sulfate. Add 6 M HCl until the mixture is acidic to litmus. If cyanide remains a deep blue precipitate forms. When the test is negative the aqueous solution is washed into the drain with 50 times its volume of water.

2.2.3 1-octaneselenol (4a)



A suspension of 1,2-dioctyldiselane (**3a**, 40.4 g, 105 mmol, 1.0 equiv) in 2-propanol (100 mL) was heated under reflux until dissolution occurred. Hypophosphorous acid (50% w/v aqueous solution; 20.8 g, 17.3 mL, 157.5 mmol, 1.5 equiv) was added. Heating at reflux was continued for 17 h whereupon the reaction mixture was allowed to cool to room temperature. H_2O (315 mL) and 40–60 petrol (315 mL) were added and the layers separated. The aqueous layer was extracted with 40–60 petrol (100 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo. The residual oil was purified by short path distillation to give 1-octaneselenol (**4a**, 38.0 g, 197 mmol, 94%) as a colourless oil bp 81–85 °C/20 mmHg; lit.[3] bp 117–120 °C/42 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.58 (2H, q, J = 7.1, C1H_2), 1.69 (2H, quint, J = 7.5, C2H_2), 1.40–1.33 (2H, m, CH_2), 1.33–1.22 (8H, m, 4 × CH_2), 0.88 (3H, t, J = 7.0, C8H_2), –0.69 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.1 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 22.7 (CH_2), 17.7 (CH_2; $^1J_{Se–C}$ = 47.4), 14.1 (CH_3). IR (thin film): ν = 2321 w (SeH) cm^{-1}. LRMS (EI$^+$ mode): m/z = 194 [M$^+$, 100%]. HRMS (EI$^+$ mode): m/z = 194.0580 [M$^+$, 100%]; calculated for $C_8H_{18}Se$ [M$^+$]: m/z = 194.0574.

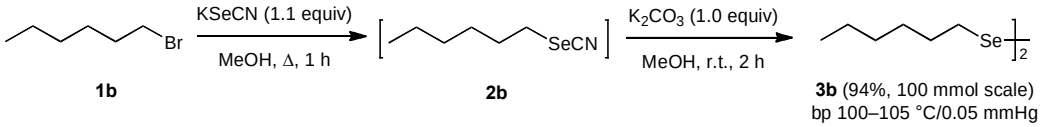
2.3 One-pot synthesis of 1,2-dioctyldiselane (3a)



A black suspension of selenium (100 mesh, 13.03 g, 165 mmol, 1.1 equiv) and potassium cyanide (11.72 g, 180 mmol, 1.2 equiv) in methanol (100 mL) was stirred at ambient temperature for 1 h forming a pale grey turbid reaction mixture containing potassium selenocyanate. 1-Bromooctane (29.0 g, 150 mmol, 1.0 equiv) was added to the reaction mixture in one portion and the resulting grey suspension heated under reflux for 1 h forming a yellow/brown suspension. Anhydrous potassium carbonate (20.7 g, 150 mmol, 1.0 equiv) was added to the reaction mixture in one portion and the resulting yellow suspension heated under reflux for 2 h. The reaction mixture was poured into ice–water (300 mL) and the mixture extracted with hexanes (2 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo to give the crude title compound that was purified by short path distillation. A yellow malodorous forerun (ca 3 g) was collected in a liquid nitrogen cooled receiver at a pot temperature of 60 °C (1.0 mm Hg). After changing the receiver, the 1,2-dioctyldiselane **3a** (26.52 g, 69.0 mmol, 92%) distilled at 150–155 °C/0.03 mmHg. KOH (8.4 g, 150 mmol, 1.0 equiv) dissolved in H_2O (ca. 10 mL) can be added to the crude 1-octaneselenocyanate instead of anhydrous K_2CO_3.

2.4 One-pot synthesis of 1,2-dialkyldiselanes (3b–3i)

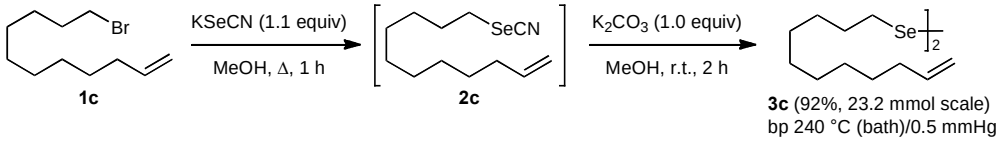
2.4.1 1,2-Dihexyldiselane (3b)



The title compound was prepared in 94% yield on a 100 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by

short-path distillation to give 1,2-dihexyldiselane (**3b**) as an orange oil: bp 100–105 °C/0.05 mmHg; lit.[1] bp 150–152 °C/3 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.91 (4H, app t, J = 7.3, C1H_2), 1.73 (4H, app quint, J = 7.6, C2H_2), 1.43–1.35 (4H, m, 2 × CH_2), 1.35–1.25 (8H, m, 4 × CH_2), 0.89 (6H, t, J = C6H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.5 (2C, CH_2), 31.1 (2C, CH_2), 30.4 (2C, C1H_2; $^{1}J_{Se–C}$ = 70.8), 29.3 (2C, CH_2), 22.7 (2C, CH_2), 14.2 (2C, C6H_3). ^{1}H NMR spectroscopic data (60 MHz) have been reported[4] for diselane **3c**.

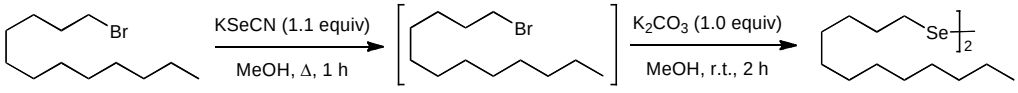
2.4.2 1,2-Di(undec-10-en-1-yl)diselane (3c).



1c **2c**
3c (92%, 23.2 mmol scale)
bp 240 °C (bath)/0.5 mmHg

The title compound was prepared in 92% yield on a 23.2 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by kugelrohr distillation to give diselane **3c** as an orange oil that solidified in the freezer (–20 °C): bp 240 °C (oven)/0.5 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.81 (2H, ddt, J = 16.9, 10.2, 6.7, C10H), 4.99 (2H, dq, J = 16.9, 1.8, C11H_{trans}), 4.95–4.91 (2H, m, C11H_{cis}), 2.91 (4H, app t, J = 7.5, C1H_2), 2.04 (4H, app q, J = 7.1, C9H_2), 1.72 (4H, quint, J = 7.4, C2H_2), 1.42–1.33 (8H, m, 4 × CH_2), 1.33–1.26 (16H, m, 8 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.3 (2C, C10H), 114.3 (2C, C11H_2), 34.0 (2C, CH_2), 31.1 (2C, CH_2), 30.4 (2C, CH_2), 29.7 (2C, CH_2), 29.6 (2C, CH_2), 29.6 (2C, CH_2), 29.3 (2C, CH_2), 29.1 (2C, CH_2).

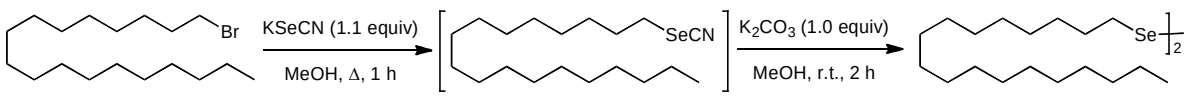
2.4.3 1,2-Didodecyldiselane (3d).



1d **2d**
3d (89%, 100 mmol scale)
mp 28–30 °C (2-PrOH)

The title compound was prepared in 89% yield on a 100 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by crystallization from 2-propanol to give 1,2-didodecyldiselane (**3d**) as yellow needles: mp 28–30 °C; lit.[5] mp 29.5–30.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.91 (4H, app t, J = 7.4, C1H_2), 1.72 (4H, quint, J = 7.5, C2H_2), 1.42–1.33 (4H, m, 2 × CH_2), 1.33–1.20 (28H, m, 2 × CH_2), 0.88 (6H, t, J = 6.9, C12H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.1 (2C, CH_2), 31.1 (2C, CH_2), 30.4 (2C, CH_2), 29.8 (2C, CH_2), 29.8 (2C, CH_2), 29.8 (2C, CH_2), 29.7 (2C, CH_2), 29.5 (2C, CH_2), 29.3 (2C, CH_2), 22.9 (2C, CH_2), 14.3 (2C, CH_3). ^{1}H NMR spectroscopic data (60 MHz) have been reported[5] for diselane **3d**.

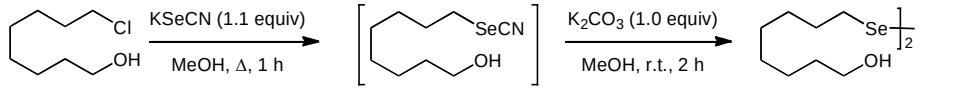
2.4.4 1,2-Dioctadecyldiselane (3e)



1e **2e**
3e (59%, 50 mmol scale)
mp 64–66 °C (acetone)

The title compound was prepared in 59% yield on a 50 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by crystallization from acetone to give 1,2-dioctadecyldiselane (**3e**) as pale yellow plates: mp 64–66 °C; lit.[6] mp 60.0–60.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.91 (4H, app t, J = 7.4, C1H_2), 1.72 (4H, p, J = 7.4, 1H), 1.34–1.26 (4H, m, 2 × CH_2), 1.34–1.20 (52H, m, 26 × CH_2), 0.88 (6H, t, J = 6.8, C18H_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.1 (2C, CH_2), 31.1 (2C, CH_2), 30.4 (2C, CH_2), 29.9 (2C, CH_2), 29.8 (2C, CH_2), 29.8 (2C, CH_2), 29.7 (2C, CH_2), 29.5 (2C, CH_2), 29.3 (2C, CH_2), 22.9 (2C, CH_2), 14.3 (2C, CH_3).

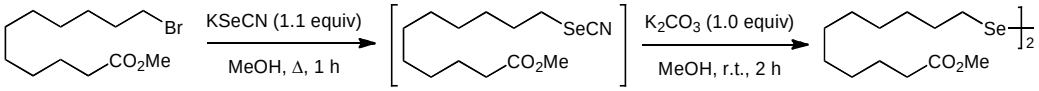
2.4.5 8,8′-Diselanediylbis(octan-1-ol) (3f).



1f **2f** **3f** (62%, 30.4 mmol scale)
mp 49–50 °C (MTBE–hexane)

The title compound was prepared in 62% yield on a 30.4 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by crystallization from MTBE–hexane to give 8,8′-diselenediylbis(octan-1-ol) (**3f**) as pale yellow solid: mp 49–50 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.62 (4H, t, J = 6.7, C1H_2), 2.90 (4H, app t, J = 7.3, C8H_2), 1.72 (4H, app quint, J = 7.4, C7H_2), 1.60–1.51 (4H, m, 2 × CH_2), 1.43–1.28 (18H, m, 9 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 63.1 (2C, C1H_2), 32.9 (2C, CH_2), 31.1 (2C, 2C, CH_2), 30.3 (2C, CH_2), 29.6 (2C, CH_2), 29.4 (2C, CH_2), 29.2 (2C, CH_2), 25.8 (2C, CH_2). IR (solid): ν = 3600–2900 br, s, 2919 s, 2852 s, 1469 m, 1411 m, 1348 m, 1261 w, 1215 w, 1172 m, 1052 s cm^{-1}. LRMS (ES^+ mode): m/z = 441 [MNa^+, 80%], 179 (100%). HRMS (ES^+ mode): m/z = 441.0791 [MNa^+, 100%]; calculated for $C_{16}H_{34}NaO_2Se_2$ [MNa^+]: m/z = 441.0784.

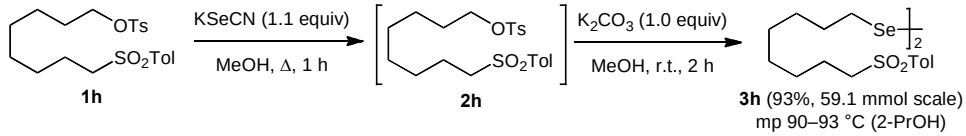
2.4.6 Dimethyl 11,11′-diselanediyldiundecanoate (3g)



1g **2g** **3g** (71%, 75 mmol scale)
mp 45–47 °C (MeOH)

The title compound was prepared in 71% yield on a 75 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by crystallization from methanol to give dimethyl 11,11′-diselanediyldiundecanoate (**3g**) as yellow plates: mp 45–47 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.66 (6H, s, 2 × CO_2Me), 2.90 (4H, app t, J = 7.4, C1H_2), 2.30 (4H, t, J = 7.6, C11H_2), 1.71 (4H, quint, J = 7.4, C2H_2), 1.61 (4H, quint, J = 7.4, C10H_2), 1.41–1.33 (4H, m, 2 × CH_2), 1.33–1.24 (20H, m, 10 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.5 (2C, CO_2Me), 51.6 (2C, CH_2), 34.2 (2C, CH_2), 31.1 (2C, CH_2), 30.4 (2C, CH_2), 29.6 (2C, CH_2), 29.6 (2C, CH_2), 29.5 (2C, CH_2), 29.4 (2C, CH_2), 29.3 (2C, CH_2), 29.2 (2C, CH_2), 25.1 (2C, CH_2). IR (solid): ν = 1737 cm^{-1} (C=O). LRMS (ES^+ mode): m/z = 581 [MNa^+, 100%]. HRMS (ES^+ mode): m/z = 581.1636 [MNa^+, 100%]; calculated for $C_{24}H_{46}NaO_4Se_2$ [MNa^+]: m/z = 581.1623.

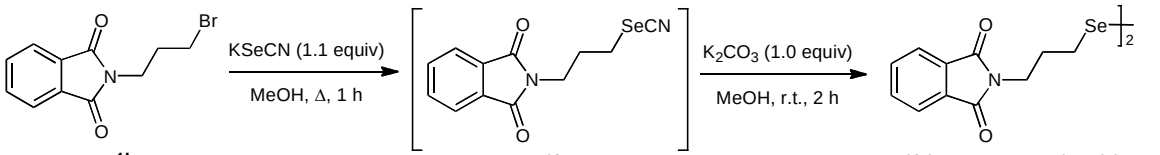
2.4.7 1,2-Bis(8-tosyloctyl)diselane (3h)



1h **2h** **3h** (93%, 59.1 mmol scale)
mp 90–93 °C (2-PrOH)

The title compound was prepared in 93% yield on a 59.1 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by trituration with 2-propanol followed by crystallization from 2-propanol (ca 200 mL) to give 1,2-bis(8-tosyloctyl)diselane (**3h**) as fine yellow needles: mp 90–93 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (4H, d, J = 8.3, ArH), 7.36 (4H, d, J = 8.1, ArH), 3.08–3.03 (4H, m, C8H_2), 2.87 (4H, t, J = 7.4, C1H_2), 2.46 (6H, s, ArCH_3), 1.73–1.65 (8H, m, 4 × CH_2), 1.39–1.30 (8H, m, 4 × CH_2), 1.30–1.23 (8H, m, 4 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7 (2C, C_{Ar}), 136.4 (2C, C_{Ar}), 130.0 (4C, C_{Ar}H), 128.2 (4C, C_{Ar}H), 56.5 (2C, C8H_2), 30.9 (2C, CH_2), 30.1 (2C, CH_2), 29.4 (2C, CH_2), 29.0 (2C, CH_2), 28.8 (2C, CH_2), 28.3 (2C, CH_2), 22.8 (2C, C1H_2), 21.7 (2C, ArCH_3). IR (solid): ν = 2926 s, 2853 m, 1597 w, 1468 m, 1410 w, 1313 s, 1301 s, 1283 s, 1267 m cm^{-1}. LRMS (ES$^+$ mode): m/z = 735 (15%), 731 (25%), 729 (15%), 719 (40%), 717 [MNa^+, 100%], 715 (90%), 713 (60%), 711 (25%). HRMS (ES$^+$ mode): m/z = 717.1060 [MNa^+, 100%]; calculated for $C_{30}H_{46}NaO_4S_2Se_2$ [MNa^+]: m/z = 717.1063.

2.4.8 2,2′-(Diselanediylbis(propane-3,1-diyl))bis(isoindoline-1,3-dione) (3i).



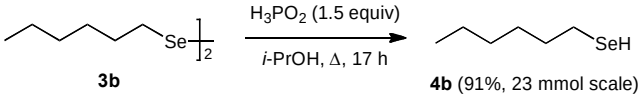
1i **2i** **3i** (80%, 93.2 mmol scale)
mp 80–83 °C (EtOAc–hexane)

The title compound was prepared in 80% yield on a 93.2 mmol scale using the general telescoped procedure for 1,2-dialkyldiselane synthesis described above. The crude product was purified by crystallization from EtOAc–hexane to give diselane **3i** as a pale yellow solid: mp 80–83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (4H, dd, J = 5.5, 3.1, ArH), (4H, dd, J = 5.5, 3.0, ArH), 3.79 (4H, t, J = 6.9, CH_2), 2.92 (4H, t, J = 7.4, CH_2), 2.13 (4H, quint, J = 7.1, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4 (4C, C=O), 134.1(4C, C_{Ar}H), 132.2 (4C, C_{Ar}), 123.4 (4C, C_{Ar}H), 37.7 (2C, CH_2), 30.0 (2C, CH_2), 26.5 (2C, CH_2). IR (solid): ν = 1700 cm^{-1} (C=O). LRMS (ES$^+$ mode): m/z = 558 [MNa^+, 100%]. HRMS (ES$^+$ mode): m/z = 558.9650 [MNa^+, 100%]; calculated for $C_{22}H_{20}N_2O_4Se_2$ [MNa^+]: m/z = 558. 9650.

2.5 General procedure for alkylselenol synthesis (**4b**-**4i**)

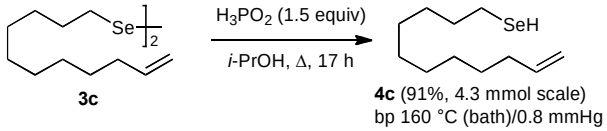
A suspension of 1,2-dialkyldiselane (1.0 equiv) in 2-propanol (1 M solution) was heated under reflux until dissolution occurred. Hypophosphorous acid (50% w/v aqueous solution; 1.5 equiv) was added and the resulting solution heated under reflux for 17 h. The reaction mixture was allowed to cool to room temperature and the solvent removed in vacuo. H_2O (3 mL per mmol of diselane) and hexanes (3 mL per mmol of diselane) were added, the layers separated, and the aqueous layer extracted with hexanes (2 × 3 mL per mmol of diselane). The combined organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo to give the crude title compound that was purified as described for each example.

2.5.1 1-Hexaneselenol (4b)



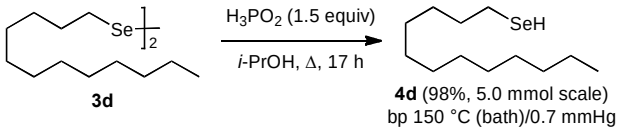
The title compound was prepared in 91% yield on a 22.8 mmol scale using the general procedure for selenol synthesis described above. The crude product was purified by short-path distillation to give hexane-1-selenol (**4b**) as a colourless oil: bp 35–36 °C/1.2 mmHg; lit.[7] bp 82 °C/20 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.58 (2H, q, J = 7.1, C1H$_2$), 1.69 (2H, app quint, J = 7.3, C2H$_2$), 1.41–1.33 (2H, m, CH$_2$), 1.33–1.22 (4H, m, 2 × CH$_2$), 0.88 (3H, t, J = 7.0, C6H$_3$), –0.69 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.1 (CH$_2$), 31.3 (CH$_2$), 29.4 (CH$_2$), 22.7 (CH$_2$), 17.9 (CH$_2$, $^{1}J_{Se–C}$ = 47.4, C1H$_2$), 14.2 (C6H$_3$).

2.5.2 Undec-10-ene-1-selenol (4c).



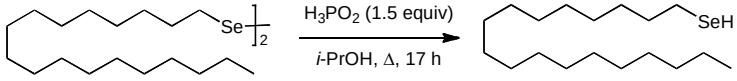
The title compound was prepared in 91% yield on a 4.3 mmol scale using the general procedure for selenol synthesis described above. The crude product was purified by kugelrohr distillation to give undec-10-ene-1-selenol (**4c**) as a colourless oil that solidified in the freezer (–20 °C): bp 160 °C (oven)/0.8 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.77 (1H, ddt, J = 16.9, 10.0, 6.7, C10H), 4.99–4.93 (1H, m, C11H$_{trans}$), 4.92–4.87 (1H, m, C11H$_{cis}$), 2.55 (2H, app q, J = 7.1, C1H$_2$), 2.01 (2H, q, J = 7.2, C9H$_2$), 1.67 (2H, quint, J = 7.3, C2H$_2$), 1.41–1.30 (4H, m, 2 × CH$_2$), 1.30–1.21 (8H, m, 4 × CH$_2$), –0.73 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.0 (C10H), 114.2 (C11H$_2$), 34.1 (CH$_2$), 33.8 (CH$_2$), 29.6 (CH$_2$), 29.5 (CH$_2$), 29.5 (CH$_2$), 29.1 (CH$_2$), 29.0 (CH$_2$), 28.9 (CH$_2$), 17.7 (CH$_2$, $^{1}J_{Se–C}$ = 47.4). IR (thin film): ν = 2037 w (SeH), 1640 w (C=C) cm^{-1}.

2.5.3 1-Dodecaneselenol (4d).



The title compound was prepared in 98% yield on a 5.0 mmol scale using the general procedure for selenol synthesis described above. The crude product was purified by kugelrohr distillation to give dodecane-1-selenol as a colourless oil: bp 150 °C (oven)/0.7 mmHg; lit.[8] bp 160–170 °C/10 mmHg. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.55 (2H, app q, J = 7.1, C1H$_2$), 1.67 (2H, quint, J = 7.2, C2H$_2$), 1.38–1.30 (2H, m, CH$_2$), 1.30–1.18 (16H, m, 8 × CH$_2$), 0.86 (3H, t, J = 6.9, C12H$_3$), –0.73 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.1 (CH$_2$), 32.0 (CH$_2$), 29.8 (CH$_2$), 29.74 (CH$_2$), 29.7 (CH$_2$), 29.7 (CH$_2$), 29.6 (CH$_2$), 29.5 (CH$_2$), 29.1 (CH$_2$), 22.8 (CH$_2$), 17.8 (CH$_2$, $^{1}J_{Se–C}$ = 47.2), 14.2 (C12H$_3$).

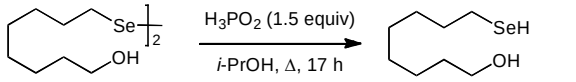
2.5.4 1-Octadecaneselenol (4e)



3e **4e** (95%, 3.81 mmol scale)
mp 36–39 °C (acetone)

The title compound was prepared in 95% yield on a 2.0 mmol scale using the general procedure for selenol synthesis described above. The crude product was purified by crystallization from the crude reaction mixture followed by washing with cold acetone (15 mL) to give 1-octadecaneselenol (**4e**) as a colourless solid: mp 36–39 °C; lit.[9] mp 36–40 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.59 (2H, app q, J = 7.1, C1H_2), 1.70 (2H, app quint, J = 7.3, C2H_2), 1.41–1.32 (2H, m, C2H_2), 1.32–1.21 (28H, m, 14 × CH_2), 0.88 (3H, t, J = 6.9, C18H_3), –0.69 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 22.9 (CH_2), 17.9 (CH_2), 14.3 (CH_3).

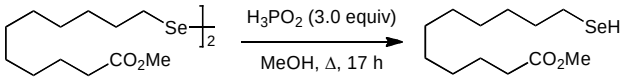
2.5.5 8-Hydroselenooctan-1-ol (4f)



3f **4f** (87%, 5.0 mmol scale)
bp 160 °C (bath)/0.8 mmHg

The title compound was prepared in 87% yield on a 5.0 mmol scale using the general procedure for selenol synthesis described above. The crude product was purified by kugelrohr distillation to give 8-hydroselenooctan-1-ol (**4f**) as a colourless oil: bp 160 °C (oven)/0.8 mmHg; mp ca. 18 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.63 (2H, t, J = 6.6, C8H_2), 2.58 (2H, q, J = 7.1 Hz, C1H_2), 1.69 (2H, quint, J = 7.3, C2H_2), 1.66 (1H, s, OH), 1.55 (2H, quint, J = 6.7, C7H_2), 1.42– 1.26 (8H, m, 4 × CH_2) –0.69 (1H, t, J = 6.8, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 63.1 (C8H_2), 34.1 (CH_2), 32.8 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.0 (CH_2), 25.8 (CH_2), 17.9 (CH_2). IR (thin film): ν = 3300 br (OH), 2305 w (SeH) cm^{-1}.

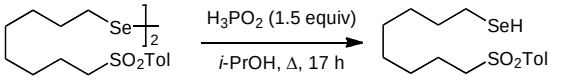
2.5.6 Methyl 11-hydroselenoundecanoate (4g)



3g **4g** (89%, 1.8 mmol scale)
bp 190 °C (bath)/0.8 mmHg

The title compound was prepared in 89% yield on a 1.80 mmol scale using the general procedure for selenol synthesis described above except that the reaction was performed in MeOH as solvent using 3.0 equiv of H_3PO_2. The crude product was purified by kugelrohr distillation to give methyl 11-hydroselenoundecanoate (**4g**) as a colourless oil: bp 190 °C (oven)/0.8 mmHg; mp ca. 20 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.66 (3H, s, CO_2Me), 2.58 (2H, q, J = 7.0, C1H_2), 2.31 (2H, t, J = 7.6, C10H), 1.63 (2H, quint, J = 7.2 Hz, CH_2), 1.66–1.57 (2H, m, CH_2), 1.42–1.23 (12H, m, 6 × CH_2), –0.69 (1H, t, J = 6.9 Hz, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2 (C), 51.4 (CO_2Me), 34.0 (CH_2), 34.0 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 24.9 (CH_2), 17.7 (CH_2 , $^{1}J_{Se–C}$ = 47.5). IR (thin film): ν = 2306 w (SeH), 1737 s (C=O) cm^{-1}.

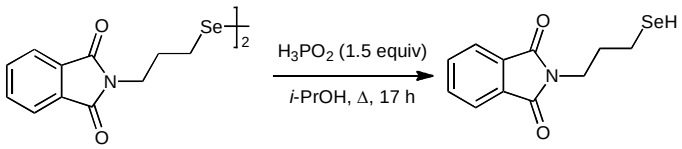
2.5.7 8-Tosyloctane-1-selenol (4h)



3h **4h** (97%, 24.4 mmol scale)
mp 60–61 °C (2-PrOH)

The title compound was prepared in 97% yield on a 24.4 mmol scale using the general procedure for selenol synthesis described above. The product crystallized directly from the reaction mixture on cooling to room temperature and was collected by suction filtration. After washing with cold 2-propanol (2 × 25 mL) 8-tosyloctane-1-selenol was obtained as fine white needles: mp 60–61 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (2H, d, J = 8.4, ArH), 7.36 (2H, d, J = 7.9, ArH), 3.08–3.03 (2H, m, C8H_2), 2.56 (2H, q, J = 7.0 Hz, C1H_2), 2.46 (3H, s, ArCH_3), 1.73–1.63 (4H, m, 2 × CH_2), 1.39–1.29 (4H, m, 2 × CH_2), 1.29–1.22 (4H, m, 2 × CH_2), –0.69 (1H, t, J = 6.9, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.6 (C_{Ar}), 136.3 (C_{Ar}), 129.9 (2C, C_{Ar}H), 128.1 (2C, C_{Ar}H), 56.3 (C8H_2), 33.8 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 28.5 (CH_2), 28.2 (CH_2), 22.7 (CH_2), 21.7 (ArCH_3), 17.6 (C1H_2). IR (solid): ν = 2971 m, 2916 s, 2849 s, 1595 s, 1492 w, 1468 s, 1403 m, 1330 m, 1281 s, cm^{-1}. LRMS (ES^+ mode): m/z = 373 (24%), 372 (20%), 371 [MNa^+, 100%], 370 (10%), 369 (50%). HRMS (ES^+ mode): m/z = 371.0546 [MNa^+, 100%]; calculated for $C_{15}H_{24}NaO_2SSe$ [MNa^+]: m/z = 371.0554.

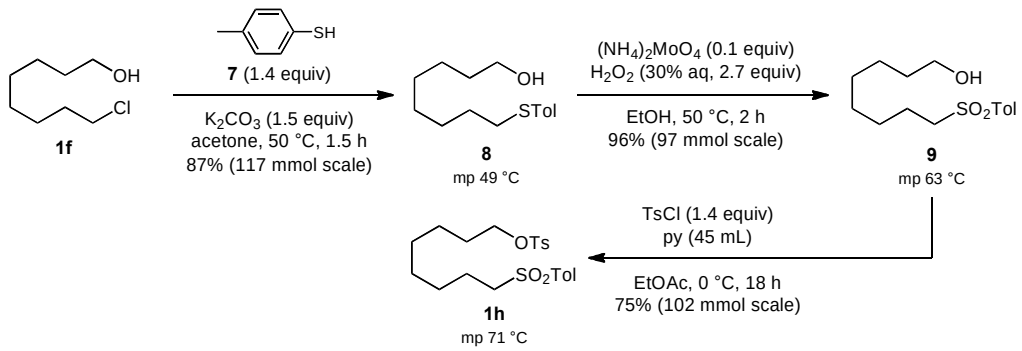
2.5.8 2-(3-Hydroselenopropyl)isoindoline-1,3-dione (4i)



3i **4i** (91%, 5.0 mmol scale)
mp 50 °C (2-PrOH)

The title compound was prepared in 91% yield on a 5.0 mmol scale using the general procedure for selenol synthesis described above. The product crystallized directly from the reaction mixture on cooling to room temperature and was collected by suction filtration. After washing with cold 2-propanol (2 × 10 mL) the selenol **4i** was obtained as an off-white solid: mp 50–54 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (2H, J = 7.0, 3.9, ArH), 7.71 (2H, dq, J = 7.0, 3.9, ArH), 3.79 (2H, t, J = 6.8, CH_2), 2.58 (2H, q, J = 7.2, CH_2), 2.10 (2H, app quint, J = 7.0, CH_2), –0.44 (1H, t, J = 7.2 Hz, SeH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4 (2C; C=O), 134.1 (2C; C_{Ar}H), 132.1(2C, C_{Ar}), 123.3 (2C, C_{Ar}H), 37.6 (CH_2), 32.9 (CH_2), 14.4 (CH_2). IR (solid): ν = 2302, w (SeH), 1700, s (C=O) cm^{-1}.

2.6 Synthesis of 8-Tosyloctyl 4-methylbenzenesulfonate (1h)



2.6.1 8-(p-Tolylthio)octan-1-ol (**8**).

To a suspension of K_2CO_3 (24.0 g, 174 mmol, 1.5 equiv) in acetone (75 mL) at room temperature was added a solution of thiocresol (**7**, 20.0 g, 161 mmol, 1.4 equiv) in acetone (30 mL) followed by a solution of 8-chloro-1-octanol **1f** (19.2 g, 117 mmol, 1.0 equiv) in acetone (30 mL). A mild exotherm was observed and the reaction temperature increased to 45 °C where it remained for 10 min. When the temperature reached 35 °C the resulting suspension was heated at 50 °C for 1.5 h. After cooling to room temperature, the reaction mixture was filtered through a celite pad washing the residual solids with acetone (75 mL). The filtrate was concentrated in vacuo, the residue partitioned between Et_2O (150 mL) and H_2O (50 mL), the layers separated and the organic layer washed with 5 M NaOH (4 × 50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated in vacuo to give a solid that was crystallized from hexane to give 8-(p-tolylthio)octan-1-ol (**8**, 25.7 g, 102 mmol, 87%) as colourless plates: mp 49–51 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 (2H, d, J = 8.2, ArH), 7.09 (2H, d, J = 7.9, ArH), 3.63 (2H, q, J = 6.3, C1H_2), 2.87 (2H, t, J = 7.4, C8H_2), 2.31 (3H, s, ArCH_3), 1.66–1.52 (4H, m, 2 × CH_2), 1.41 (2H, app quint, J = 7.4, C2H_2), 1.39–1.26 (6H, m, 3 × CH_2), 1.25 (1H, t, J = 5.4, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.9 (C_{Ar}), 133.1(C_{Ar}), 129.8 (2C, C_{Ar}H), 129.7 (2C, C_{Ar}H), 63.0 (C1H_2), 34.3 (CH_2), 32.8 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 28.8 (CH_2), 25.7 (CH_2), 21.1 (ArCH_3). IR (solid): ν = 3330 m (OH) cm^{-1}. LRMS (ES$^+$ mode): m/z = 275 [MNa^+, 100%], 253 [MH^+, 70%]. HRMS (ES$^+$ mode): m/z = 253.1614 [MH^+, 100%]; calculated for $C_{15}H_{25}OS$ [MNa^+]: m/z = 253.1621.

2.6.2 8-Tosyloctan-1-ol (**9**)

A suspension of ammonium molybdate (2.5 g, 12.8 mmol, 0.1 equiv) and hydrogen peroxide (30% aqueous; 30 mL, 265 mmol, 2.7 equiv) in EtOH (300 mL) was heated at 40 °C for 15 min forming a yellow solution. 8-(p-Tolylthio)octan-1-ol (**8**, 24.5 g, 97.1 mmol, 1.0 equiv) in EtOH (70 mL) was added dropwise via an addition funnel at a rate sufficient to keep the reaction temperature at 43–47 °C. The reaction mixture was stirred at 50 °C for 2 h, cooled to room temperature and poured onto H_2O (1 L) and extracted with MTBE (2 × 300 mL). The combined organic layers were washed with saturated $Na_2S_2O_3$ (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4) and concentrated in vacuo to give a colourless oil that was triturated with petrol to give 8-tosyloctan-1-ol (**9**, 26.6 g, 93.5 mmol, 96%) as a white solid that could be used in the subsequent O-tosylation step with no further purification. An analytical sample obtained by crystallization from EtOAc–petrol (1:1) gave sulfone **9** as white prisms: mp 63–66 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.77 (2H, dt, J = 8.2, 2.2, ArH), 7.35 (2H, dd, J = 8.1, 1.9, ArH), 3.60 (2H, td, J = 6.6, 2.9, C1H_2), 3.08–3.00 (2H, m, C8H_2), 2.44 (3H, s, ArCH_3), 1.73–1.63 (2H, m, C7H_2), 1.55–1.47 (2H, m, C2H_2), 1.45 (1H, br s, OH), 1.38–1.22 (8H, m, 4 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7 (C_{Ar}), 136.2 (C_{Ar}), 130.0 (2C, C_{Ar}H), 128.2 (2C, C_{Ar}H), 63.0 (C1H_2), 56.5 (CH_2), 32.7(CH_2), 29.1 (CH_2), 29.1 (CH_2), 28.3 (CH_2), 25.7 (CH_2), 22.8 (CH_2), 21.8 (ArCH_3). IR (solid): ν = 1275 and 1140 s (SO_2) cm^{-1}. LRMS (ES$^+$ mode): m/z = 307

[MNa^+, 100%], 285 [MH^+, 40%]. HRMS (ES^+ mode): m/z = 285.1530 [MH^+, 100%]; calculated for $C_{15}H_{25}O_3S$ [MNa^+]: m/z = 285.1519.

2.6.3 8-Tosyloctyl 4-methylbenzenesulfonate (**1h**)

Tosyl chloride (27.5 g, 144 mmol, 1.4 equiv) in EtOAc (40 mL) was added dropwise via an addition funnel to a solution of 8-tosyloctan-1-ol (**9**, 28.9 g, 102 mmol, 1.0 equiv) in pyridine (45 mL) at 0 °C at a rate sufficient to keep the reaction temperature at 0–5 °C. The resulting white suspension was stirred at 0 °C for 18 h. The reaction was quenched with H_2O (3 mL), stirred at room temperature for 5 min, poured onto H_2O (280 mL) and extracted with EtOAc (2 × 75 mL). The combined organic layers were washed with 6 M HCl (2 × 50 mL), H_2O (50 mL) and saturated $NaHCO_3$ (50 mL), dried (Na_2SO_4) and concentrated in vacuo to give a colourless oil that was triturated with Et_2O (50 mL) to give a white solid. The solid was crystallized from MTBE to give 8-tosyloctyl 4-methylbenzenesulfonate (**1h**, 34.1 g, 77.7 mmol, 75%) as a colourless crystalline solid: mp 71–75 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.80–7.60 (4H, m, ArH), 7.39–7.31 (4H, m, ArH), 4.00 (2H, t, J = 6.4, C1H_2), 3.07–3.00 (2H, m, C8H_2), 2.46 (3H, s, ArCH_3), 2.45 (3H, s, ArCH_3), 1.71–1.57 (4H, m, C2H_2/C7H_2), 1.35–1.17 (8H, m, 4 × CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.8 (C_{Ar}), 144.7 (C_{Ar}), 136.2 (C_{Ar}), 133.1 (C_{Ar}), 130.0 (2C, $C_{Ar}H$), 129.9 (2C, $C_{Ar}H$), 128.1 (2C, $C_{Ar}H$), 127.9 (2C, $C_{Ar}H$), 70.6 (C1H_2), 56.4 (C8H_2), 28.8 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 25.2 (CH_2), 22.7 (CH_2), 21.7 (2C, 2 × ArCH_3). IR (solid): ν = 1351 s, 1172 s, 1141 s cm^{-1}. LRMS (ES^+ mode): m/z = 461 [MNa^+, 100%]. HRMS (ES^+ mode): m/z = 461.1437 [MNa^+, 100%]; calculated for $C_{22}H_{30}NaO_5S_2$ [MNa^+]: m/z = 461.1427.

3. References

(1) Stoner, G. G.; Williams, R. W. n-Alkyl Diselenides. J. Am. Chem. Soc. **1948**, 70, 1113–1114.

(2) Nakamura, T.; Yasuda, S.; Miyamae, T.; Nozoye, H.; Kobayashi, N.; Kondoh, H.; Nakai, I.; Ohta, T.; Yoshimura, D.; Matsumoto, M. Effective Insulating Properties of Autooxidized Monolayers Using Organic Ditellurides. J. Am. Chem. Soc. **2002**, 124, 12642–12643.

(3) Lapkin, I. I.; Pavlova, N. N. Reactions of α-chloro ethers in the presence of zinc. VII. Reaction of alkylselenols and selenophenols with chloromethyl methyl ether in the presence of zinc. J. Org. Chem. USSR (English Translation) **1968**, 4, 782.

(4) Zhong, P.; Guo, M.-P. Preparation of Diselenides by the Oxidation of Selenols Using Trichloroisocyanuric Acid. Synth. Commun. **2001**, 31, 1507–1510.

(5) Lewicki, J. W.; Gunther, W. H. H.; Chu, J. Y. C. Synthesis of symmetrical diselenides from aliphatic and aromatic aldehydes. J. Org. Chem. **1978**, 43, 2672–2676.

(6) Rebane, E. No Title. Ark. Kemi **1966**, 25, 363–366.

(7) Krief, A.; Dumont, W.; Robert, M. Synthesis of Hexylselenol and Hexylselenides from Hexylthiol Involving -Hexylthiolanium Salts. Synlett **2006**, 2601–2604.

(8) Stewart, W. T. California Research Corp. Production of Selenomercaptans. US 2,510,765, **1950**.

(9) Stewart, W. T.; Clayton, J. O., California Research Corp. Stabilized oxidizable hydrocarbon oil. US 2,543,074, **1951**.