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Design, Synthesis, Application and Recovery of a Minimally Fluorous Diaryl Diselenide for the Catalysis of Stannane-Mediated Radical Chain Reactions

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Abstract: The synthesis of a minimally fluorous (52% F) diaryl diselenide is described. On reduction *in situ* with tributylstannane this diselenide provides a fluorous selenol which is effective in inhibiting a range of stannane-mediated radical rearrangements, including a cyclopropylcarbinyl ring opening. A method for the recovery of the fluorous diselenide involving continuous extraction in a modified, cooled continuous extractor is described.

Keywords: Radicals and radical reactions; Catalysis; Selenium and compounds; Fluorine and compounds

For several years we have been interested in the catalysis of stannane-mediated chain reactions by benzeneselenol.[1-6] In this chemistry the conveniently handled solid diphenyl diselenide is first reduced *in situ* by the stannane, according to the stoichiometry set out in Eq. 1.[5] In this manner any preparation and handling of benzeneselenol itself is avoided.

$$PhSeSePh + Bu_3SnH \rightarrow PhSeH + Bu_3SnSePh \qquad \text{Eq. 1}$$

A radical chain sequence comprised of the following propagation steps (Eqs 2-4) may then be set up

$$A\text{-}X + Bu_3Sn\bullet \rightarrow A\bullet + Bu_3Sn\text{-}X \qquad \text{Eq. 2}$$

$$A\bullet + PhSe\text{-}H \rightarrow A\text{-}H + PhSe\bullet \qquad \text{Eq. 3}$$

$$PhSe\bullet + Bu_3Sn\text{-}H \rightarrow PhSe\text{-}H + Bu_3Sn\bullet \qquad \text{Eq. 4}$$

in which the stannyl radical acts in the usual manner to abstract the halogen or pseudohalogen from the substrate, the selenol acts as hydrogen donor, and the chain is carried by the selenyl radical abstracting hydrogen from the stannane. The rate constant for the trapping of primary alkyl radicals by benzeneselenol[7,8] is some five hundred times faster than that for trapping by tributyltin hydride[9] under identical conditions of temperature and concentration. It is therefore readily appreciated that even 5 mol% of selenol, w.r.t. the stannane will lead to a twenty five fold increase in the rate of trapping of A• in the above sequence. The bond dissociation energy of the PhSe-H bond has been determined to be 78±4 kcal.mol^{-1},[10] whilst the most recent value for that of the Sn-H bond in trimethylstannane is 79 kcal.mol^{-1}.[11] The crucial chain transfer step (Eq. 4) is therefore seen to be, at worst, modestly endothermic; it is driven in the forward direction by the continual removal of the stannyl radical according to Eq. 2.

Taking advantage of this sequence we have been able to suppress a number of relatively slow radical rearrangements.[1] Likewise we have succeeded in cleaning up the cyclizations of aryl and vinyl radicals by suppressing the slow homoallyl and neophyl rearrangements, respectively, which follow the initial rapid cyclizations.[3,5] Our present goal is the suppression of rapid rearrangements, especially the cyclopropylcarbinyl type ring openings.[12] Given the rate constants for the ring opening of the cyclopropylmethyl radical[13] and for the trapping of primary alkyl radicals by benzeneselenol,[8] it is easily

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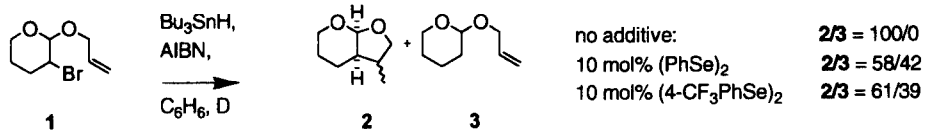
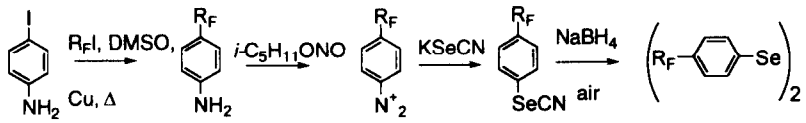
determined that molar concentrations of selenol will be required to obtain a 90% yield of the trapped product. Self-evidently, such concentrations can no longer be considered catalytic. Moreover they lead to the question of how the expensive selenol, or diselenide, may be recovered and recycled and the reaction products purified. We reasoned that the answer to these problems lay in the use of a fluorous areneselenol that, after the reaction, could be extracted into a fluorous phase.[14-16] Furthermore we reasoned that, because the rate of trapping of alkyl radicals by benzeneselenol approaches the diffusion controlled limit, any effects of the fluorous chain would be relatively minimal. This would then obviate the need for an insulating spacer between the fluorous chain and the areneselenol, such as is commonly employed with other fluorous reagents,[14] and so considerably simplify the synthesis. In order to verify this assumption we first took the precaution of preparing the known[17] bis(4-trifluoromethylphenyl) diselenide and testing its ability, following *in situ* reduction to the selenol, to inhibit a standard rearrangement. As seen from Scheme 1, the propensity of this selenol for hydrogen donation is only marginally lower than that of benzeneselenol itself. This slight loss of activity was considered a reasonable price to pay for the abbreviated synthesis of spacer free fluorous selenols and diselenides.



Scheme 1

We began with the intention of preparing a diselenide containing around 60% F by weight as this is usually thought of as the threshold for efficient extraction from an organic into a fluorous phase.[16,18] This was achieved (Scheme 2) by the copper mediated coupling of 4-iodoaniline with perfluorodecyl iodide, giving the fluorous aniline **4a**. Treatment with isoamyl nitrite then provided the diazonium salt **5a**, which, on exposure to potassium selenocyanate afforded **6a**. Finally, borohydride reduction then exposure to air yielded the yellow crystalline diselenide **7a**, with its 59% fluorous character.



4a-c **5a-c** **6a-c** **7a-c**

a:$R_F = C_{10}F_{21}$; **b**:$R_F = C_8F_{17}$; **c**:$R_F = C_6F_{13}$;

Scheme 2

Unfortunately, **7a**, with a molecular weight of 1346, proved to be insoluble in most organic and fluorous solvents. Clearly this substance was never going to provide the molar concentrations of selenol required to efficiently trap cyclopropylcarbinyl radicals. The bis(4-perfluorooctylphenyl) diselenide **7b** was next prepared by the same route. It had molecular weight of 1146, was 56% fluorous, and was somewhat more, but still insufficiently soluble. Finally, the perfluorohexyl analogue **7c** was prepared and was found to have a solubility satisfactory for our purposes. Unfortunately, with its reduced fluorine content (52%), it was not fluorous enough to permit efficient fluorous extraction. This type of problem is not uncommon in the new and rapidly evolving field of fluorous reagents and protecting groups. In effect, in order to have a partition co-efficient such that extraction is efficient one or more perfluoroalkyl chains of a considerable size have to be attached to the substrate, thereby significantly increasing the molecular weight.[19,20] This in turn means that the solubility of many fluorous species can be limited, especially in organic and partially fluorous solvents such as benzotrifluoride.[21] These elevated molecular weights can also lead to line broadening in NMR spectra because of reduced tumbling and, so, less efficient relaxation.[21] This

phenomenon is obviously less of a problem with fluorous catalysts, which were the initial focus in the area, as much lower concentrations are then required.

We reasoned that the low partition co-efficient of only moderately fluorous substrates might readily be overcome by use of a semi-micro continuous extraction apparatus in which a less dense solvent is extracted by a more dense one. The flaw in this logic was soon revealed on attempted extraction of a dichloromethane solution of a fluorous substrate by perfluoromethylcyclohexane using the minimal apparatus, such as is found in many organic laboratories, illustrated in Figure 1a. In effect, as the extraction proceeds, the apparatus becomes gradually hotter and the dichloromethane phase is not simply extracted by the fluorous phase but also begins to dissolve in it.[22] In the cooler return arm of the apparatus the two solvents again separate into two phases and the lighter dichloromethane phase is swept over, together with its non-fluorous solutes, into the receiver flask. Separation is therefore not achieved. To overcome this problem we have constructed a jacketed version of the apparatus, as shown in Figure 1b. In this very simple modification cold water is circulated through the cooling jacket such that the two phases remain cold and immiscible.[23] The apparatus illustrated in Figure 1b was constructed so as to allow supervision free operation over a period of hours. However, we also find that if the extraction period is relatively short, as is often the case, it is sufficient to wrap the extraction arm of the simple apparatus (Figure 1a) with cloth soaked in cold water, with periodic replacement.

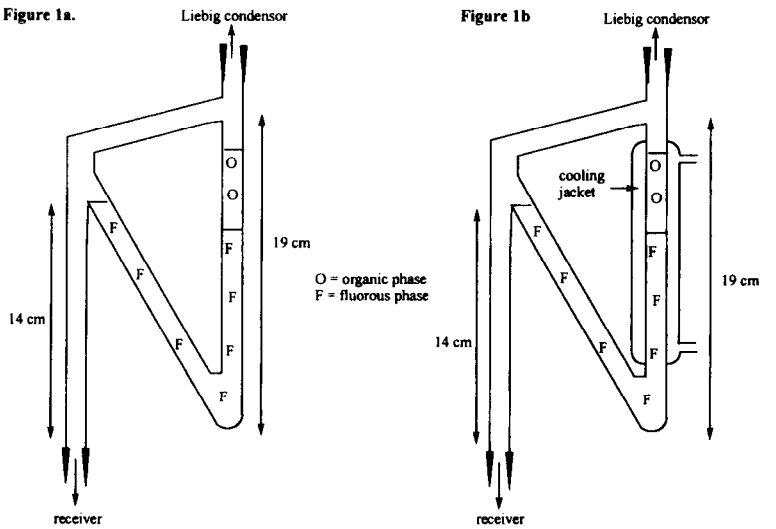


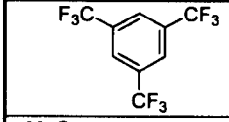
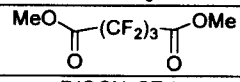
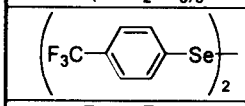
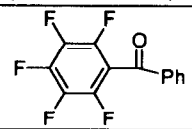
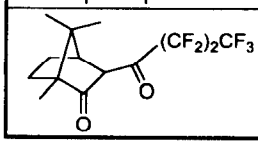
Figure 1. Classical (Fig 1a) and Jacketed (Fig 1b) Continuous Extractors

To test the viability of this apparatus we selected several minimally fluorous compounds, none of which were readily extracted in the conventional manner, and determined their partition coefficients between perfluoromethylcyclohexane and dichloromethane. They were then dissolved in dichloromethane and placed in the apparatus of Figure 1b and extracted with perfluoromethylcyclohexane. After a period of 2 h, the extraction was halted and the transfer of the substrates to the receiver assessed (Table 1).

As seen from Table 1, substrates containing as little as 38% fluorine by weight may be recovered almost quantitatively in this manner provided that the fluorine is contained within a perfluoroalkyl chain. It is reasonably well appreciated[14-16] that perfluoroaryl groups are less "fluorous" than their aliphatic counterparts and it is therefore not surprising that pentafluorobenzophenone has a low P_{FBS} and is not well extracted. Bis(4-trifluoromethylphenyl) diselenide, with only 25% fluorine and a negligible partition coefficient, was not extracted at all and so illustrates the limits of what may be done. Two other moderately

fluorous examples were not completely extracted on the 2 h time scale but succumbed when the protocol was continued for a total of 5 h.

Table 1. Recovery of Minimally Fluorous Substances with the Cooled Continuous Extractor

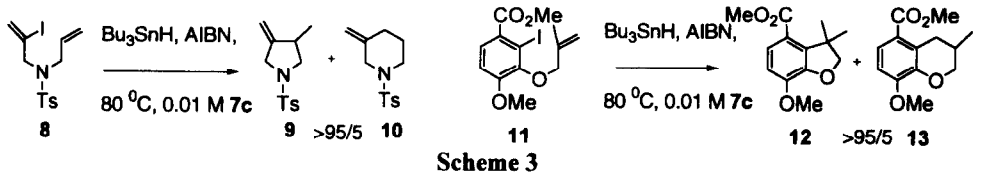
Substrate	MW	%F[a]	P_{FBS}[b]	% Recovery[c]
	282	60.6	2.30	97%
	268	42.5	0.10	63%[d]
$P(OCH_2CF_3)_3$	328	52.1	0.36	74%[d]
	224	25.4	-	0
	272	34.9	0.06	25%
	348	38.2	0.13	100%

a) % fluorine by weight; b) $P_{FBS} = c_{fluorous\ phase}/c_{other\ phase}$; c) % of fluorous substrate extracted into the fluorous phase after 2 h; d) Essentially complete recovery was achieved after a total of 5 h.

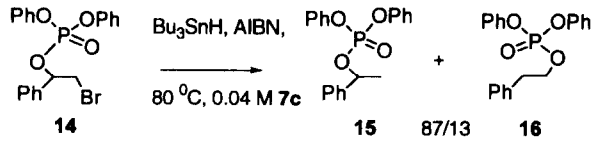
With a convenient method for the recovery of the minimally fluorous substances in hand we returned to the initial objective. In the first instance **7c** was applied to inhibition of the rapid type of 5-hexenyl radical cyclization ($k \approx 10^6 - 10^7\ s^{-1}$). A 0.07 M benzene solution of **7c**, reduced *in situ* to the selenol (Eq 1), used in conjunction with dropwise addition of tributylstannane resulted in a 1:1 mixture of the reduced and cyclized products. However, when a 0.6 M solution of **7c** was applied in the same manner inhibition of cyclization was complete and the only detectable product was **3**. At this stage the reaction mixture consists of the reaction products, the fluorous selenol, oxidized to **7c** on exposure to air, and the stannylselenide (Eq 1). Before the fluorous extraction can be conducted it is necessary to convert this latter substance back to the selenol or the diselenide. After some experimentation we discovered that a convenient way of achieving this transformation was to heat the reaction mixture with benzoyl peroxide; a protocol introduced in the non-fluorous series by Schiesser.[24] Subsequently, the volatiles were removed under vacuum and the residue taken up in dichloromethane or toluene and extracted for several hours in the jacketed continuous extractor with perfluoromethylcyclohexane. Concentration of the fluorous phase yielded yellow crystalline **7c** in >90% yield, while the organic phase contained the desired products which were purified in the usual way by chromatography over silica gel.

We next applied **7c** to the inhibition of a several stannane-mediated radical rearrangements as set out in Schemes 3 and 4. These were the homoallyl and neophyl rearrangements ($k \approx 10^4\ s^{-1}$)[25] which typically complicate vinyl and aryl radical cyclizations[26-28] (Scheme 3) and a β-(phosphatoxy)alkyl rearrangement[29,30] (Scheme 4) with $k = 8 \times 10^5\ s^{-1}$.[6] As we have discussed previously,[3,5] the examples of Scheme 3 function because the selenol does not catalyze efficiently vinyl and aryl radical reductions owing to the rate constants for the trapping of such radicals by the stannane already approaching the diffusion controlled limit.[31] As such the initial 5-exo rearrangements proceed unhindered but the slower homoallyl and neophyl rearrangements of readily trapped alkyl radicals are effectively staunched. In each of these

examples **7c** was effectively recovered by treatment of the crude reaction mixture with benzoyl peroxide followed by continuous extraction.

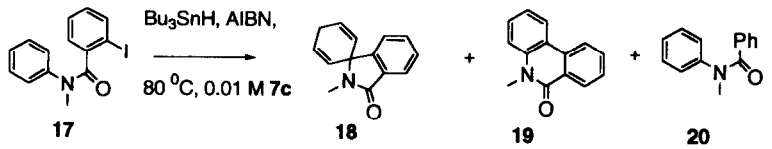


Scheme 3



Scheme 4

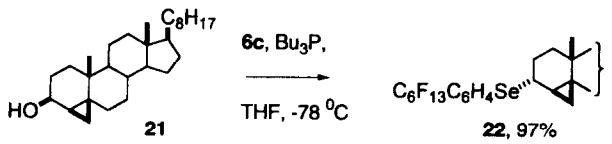
Next we investigated the ability of the reduced form of **7c** to quench resonance-stabilized radicals such as cyclohexadienyl radicals. Again as we have discussed previously, stannane-mediated radical additions, inter or intramolecular, to arenes give rise to cyclohexadienyl type radicals.[4] These radicals do not abstract hydrogen from stannanes efficiently which leads to poor chain propagation, the consequent need for large quantities of initiator, and the formation of disproportionation products. Benzeneselenol is effective in trapping such radicals as it is able to transfer hydrogen to the cyclohexadienyl radical, which leads to more efficient chain propagation, the need for reduced quantities of initiator, and cleaner reaction mixtures.[4] The example of Scheme 5 demonstrates that the fluorous selenol is also effective in catalyzing such reaction mixtures, as in its absence poor conversion of the substrate is obtained and only traces of the spirocyclic product are obtained.[4] Again **7c** was recovered by the continuous extraction protocol.



17/18/19/20 = 1/2/1/1

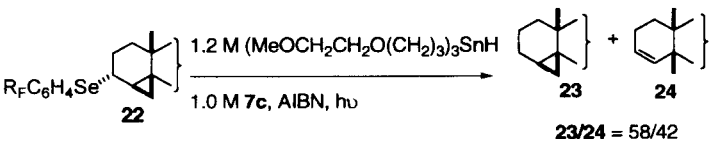
Scheme 5

Returning to the cyclopropylcarbinyl system, we constructed the fluorous selenide **22** as radical precursor by adapting methodology described by Clive for a related, non-fluorous system.[32] The fluorous selenide was selected as the radical precursor such that all of the byproducts from the radical reaction, other than those derived from the stannane, would be fluorous and convertible into diselenide **7c**. Reaction of the known cyclopropylsterol **21** with two equivalents of selenocyanate **6c** and tributylphosphine in THF at −78 °C resulted in complete conversion of the sterol (Scheme 6). After removal of the solvent, the reaction mixture was partitioned between toluene and perfluoromethylcyclohexane in the modified continuous extractor. This enabled recovery of the excess cyanate **6c** in the form of diselenide **7c** (52% F) in the fluorous phase with the steroid **22** (28% F) being retained in the organic phase. Filtration of the organic phase on silica gel then removed the phosphine derived byproducts and afforded pure **22** in 97% yield.



Scheme 6

In the radical reaction, a saturated 1 M solution of diselenide **7c** and of selenide **22** was exposed to Breslow's stannane (1.2 M) and AIBN in benzene at room temperature with sunlamp irradiation for 30 min. The crude reaction mixture was then treated with benzoyl peroxide in the usual manner, followed by continuous fluorous extraction resulting in 97% recovery of the fluorous diselenide **7c** from the fluorous phase. Filtration of the organic phase on silica gel yielded a mixture of **23** and **24**, free of selenol and stannane, in 65% yield and in the ratio 58/42 (Scheme 7). Thus, it is established that a high concentration of fluorous selenol may be used on a preparative scale to substantially inhibit a cyclopropylcarbinyl ring opening, without presenting undue problems of purification or recovery. Evidently, the 58/42 ratio obtained in the present experiment is still far from ideal; its improvement through the synthesis of a more highly soluble fluorous selenol is an ongoing goal of our research.



Scheme 7

Experimental Part

General. For general experimental protocols see footnote 1.

Jacketed Continuous Extractor. The apparatus was constructed from 1 cm o.d. Pyrex® tubing to the approximate dimensions given in figure 1b. It contains approximately ~15 mL of recoverable fluorous phase and 4-6 mL of organic phase.

Continuous Extractions (Table 1). The fluorous substrate (200 mg) was dissolved in dichloromethane (4-5 mL) and pipetted into the continuous extractor containing 15 mL of perfluoromethylcyclohexane. The apparatus was inserted between a Liebig condenser and a 10 or 25 mL round bottom flask, containing further perfluoromethylcyclohexane (5 mL), which acts as receiver. Cold water was run through the cooling jacket and the Liebig condenser, and the receiver heated such that gentle distillation ensued. After 2 h, the apparatus was allowed to cool, the receiver removed, and the two separate phases made up to equal volumes. The percentage of substrate extracted was then determined by GC analysis of the two phases.

4-Perfluorohexylbenzenediazonium Tetrafluoroborate (5c). A solution of **4c**[33] (1.5 g, 3.6 mmol) and 48% HBF_4 (1.4 mL, 10.8 mmol) in EtOH (30 mL) at 0 °C was treated with isoamyl nitrite (0.96 g, 8.2 mmol). After 30 min, a white crystalline solid was obtained by filtration and washed with water and ether several times (1.77 g, 95%). M.p. 165 ° C (decomp.); ^{1}H-NMR (d_6 acetone) δ: 8.44 (d, J = 8.9 Hz, 2H), 8.95 (d, J = 8.8 Hz, 2H); ^{19}F-NMR δ: -71.0 (m), -48.5, -45.3, -44.0 (m), -33.8 (m), -3.0 (m).

4-Perfluorohexylphenylselenocyanate (6c). To a solution of **5c** (2.5 g, 4.9 mmol) in DMF (7 mL) at 0 °C was added KSeCN (0.7 g, 6.1 mmol) in DMF (7 mL) dropwise, followed by stirring at room temperature overnight. The reaction mixture was then diluted with EtOAc (100 mL) and washed with water, brine and dried. Removal of solvent followed by column chromatography gave **6c** as a yellow solid (0.93 g, 37%). M.p. 55-57 °C; ^{1}H-NMR δ: 7.63 (d, J =8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H); ^{13}C-NMR δ: 100.2, 105.0-120.0, 127.6, 128.9, 130.4 (t), 131.8; ^{19}F-NMR δ: -53.5 (m), -50.3, -49.3, -48.9, -38.6 (m), -8.3 (m); ^{77}Se-NMR δ: 330.4. Anal. Calcd. for $C_{13}H_4F_{13}NSe$: C, 31.22, H, 0.81; Found: C, 31.36, H, 0.88.

Bis-(4-perfluorohexylphenyl) Diselenide (7c). A solution of **6c** (500 mg, 1.0 mmol) in a mixture of ether (6 mL), THF (1 mL) and EtOH (3 mL) at 0 °C was treated with $NaBH_4$ (64 mg, 1.2 mmol) followed by stirring at room temperature for 1h. Quenching with 3N HCl at 0 °C and ether extraction gave a clear yellow solution. After air was bubbled through the solution and concentration, **7c** was obtained as a yellow solid (440 mg, 92%). M.p. 95-97 °C; ^{1}H-NMR δ: 7.49 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H); ^{13}C-NMR δ: 105.0-120.0 (m), 127.8, 128.0 (t), 130.7, 135.5; ^{19}F-NMR δ: -53.8 (m), -50.4, -49.5, -49.1, -38.4 (m), -8.4 (m); ^{77}Se-NMR δ: 450.8. Anal. Calcd. for $C_{24}H_8F_{26}Se_2$: C, 30.40, H, 0.85; Found: C, 30.74, H, 0.87.

4-Perfluorodecylaniline (4a). A mixture of 4-iodoaniline (1.53 g, 7 mmol), perfluorodecyl iodide (5 g, 7.7 mmol) and copper (1.48 g, 23.3 mmol) in DMSO (8 mL) was heated to 140 °C under Ar for 6h. After filtration, the filtrate was diluted with ether (100 mL), washed with water and brine and dried over sodium sulfate. Removal of the solvent followed by column chromatography (Hexane/EtOAc, 5/1) gave **4a** as a white solid (3.0 g, 71%). M.p. 78-79 °C; ^{1}H-NMR δ: 3.96 (br s, 2H), 6.70 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H); ^{13}C-NMR δ: 106.5-109.0 (m), 110.0-112.0(m), 114.3, 118.3 (m), 128.4, 149.7; ^{19}F-NMR δ: -

53.7, -50.3, -49.5, -49.3, -48.9, -37.1 (m), -8.3 (m). Anal. Calcd. for $C_{16}H_6F_{21}N$: C, 31.44, H, 0.99; Found: C, 31.32, H, 0.90.

Bis-(4-perfluorodecylphenyl) Diselenide (7a). 12 was prepared from **4a** analogously to **7c**, via **5a** and **5b**. M.p. 142-144 °C; **7a** is insoluble in all typical NMR solvents. Anal. Calcd. for $C_{32}H_8F_{42}Se_2$: C, 28.51, H, 0.60; Found: C, 28.80, H, 0.68.

Bis-(4-perfluorooctylphenyl) Diselenide (7b). 7b was prepared analogously to **7c**, via **4b**,[33] **5b** and **6b**. M.p. 122-124 °C; ^{1}H-NMR δ: 7.49 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H); ^{13}C-NMR δ: 100-120 (m), 127.8, 130.6; ^{19}F-NMR δ: -53.7, -50.3, -49.4, -48.8, -38.3 (m), -8.3 (m). Anal. Calcd. for $C_{28}H_8F_{34}Se_2$: C, 29.29, H, 0.70; Found: C, 29.78, H, 0.69.

Standard Protocol for Recovery of the Fluorous Diselenide 7c from Stannane-Mediated Reactions. Benzoyl peroxide (0.5-1.0 equiv. of **7c**) was added to the crude reaction mixture followed by heating to reflux for 6h. The solvent was then removed under reduced pressure and the residue was dissolved in 5 mL dichloromethane or toluene. Continuous extraction in the jacketed extractor with perfluoromethylcyclohexane gave **7c** as a yellow solid in 86% to 97% yield.

Reaction of 3-Bromo-2-Allyloxytetrahydropyran (1) with Bu_3SnH and 7c. To a solution of **1**[1] (50 mg, 0.23 mmol) and **7c** (1.89 g, 2 mmol) in benzene (3.5 mL) at reflux under Ar was added a solution of Bu_3SnH (661 μL, 2.54 mmol) and AIBN (10 mg, 0.05 mmol) in benzene (1.5 mL) over 6 min followed by heating to reflux for 30 min leading to the exclusive formation of the reduction product **2**.[1] **7c** was recovered by fluorous extraction in the jacketed continuous extractor (1.63 g, 86%).

Reaction of *N*-(2-Iodo-2-propenyl)-*N*-(2-propenyl)benzenesulfonamide (8) with Bu_3SnH and 7c. A solution of **8**[5] (18.1 mg, 0.05 mmol), Bu_3SnH (29 μL, 0.11 mmol), **7c** (47 mg, 0.05 mmol) and AIBN (1.5 mg, 0.006 mmol) in benzene (5 mL) was irradiated with a 250 W sunlamp for 3h in such a way that the heat generated by the lamp maintained the solution at reflux. After removal of the solvent under reduced pressure the crude reaction mixture was analyzed by ^{1}H-NMR spectroscopy which indicated the exclusive formation of **9**.[5] Diselenide **7c** was recovered by fluorous extraction in the jacketed extractor (45 mg, 96%).

Reaction of Methyl-2-Iodo-3-Methallyloxy-4-Methoxybenzoate (11) with Bu_3SnH and 7c. A solution of **11**[1] (22 mg, 0.06 mmol), Bu_3SnH (40 μL, 0.15 mmol), **7c** (57 mg, 0.06 mmol) and AIBN (1 mg, 0.004 mmol) in benzene (6 mL) was irradiated as described for **8**. After removal of the solvent, ^{1}H-NMR spectroscopy indicated that only the exo-product **12**[1] was obtained. **7c** was recovered by fluorous extraction in the jacketed continuous extractor (55 mg, 96%).

Reaction of 2-Bromo-1-Phenylethyl-Diphenylphosphate (14) with Bu_3SnH and 7c. A solution of Bu_3SnH (120 μL, 0.45 mmol) and AIBN (1.5 mg, 0.013 mmol) in benzene (4 mL) was added over 4h with the syringe pump to a solution of **14**[34] (81 mg, 0.19 mmol) and **7c** (178 mg, 0.19 mmol) at reflux under Ar in benzene (5 mL). After a further 1h at reflux the reaction mixture was cooled to room temperature and the solvent was removed in vacuum. Examination of the crude reaction mixture by ^{1}H-NMR revealed the formation of products **15**[34] and **16**[34] in the ratio of 87:13. **7c** was recovered by fluorous extraction in the jacketed continuous extractor (160 mg, 90%).

Reaction of *o*-Iodo-*N*-Methylbenzanilide (17) with Bu_3SnH and 7c. To a 0.01M solution of **17**[4] (50 mg, 0.15 mmol) and **7c** (140 mg, 0.15 mmol) in benzene (15 mL) at reflux under Ar was added a solution of Bu_3SnH (88 μL, 0.33 mmol) and AIBN (3.2 mg, 0.022 mmol) in benzene (6 mL) by means of a syringe pump over for 48h. After a further 1h at reflux, the reaction mixture was cooled and the solvent was removed under reduced pressure. ^{1}H-NMR spectroscopy indicated that a mixture of **17**,[4] **19**,[4] **20**[4] and **18**[4] was formed in the ratio of **1:1:1:2**. **7c** was recovered by fluorous extraction in the jacketed continuous extractor (135 mg, 95%).

4β,5β-Methano-3α-(4-perfluorohexylphenylseleno)-5α-cholestane (22). A solution of **6c** (300 mg, 0.6 mmol) in dry THF (1.6 mL) was added over 1h to (**21**)[35] (120 mg, 0.3 mmol) and Bu_3P (0.15 mL, 0.6 mmol) in dry THF (1 mL) at –78 °C. The reaction mixture was then allowed to warm to room temperature and stirred for 4h. Removal of the solvent followed by column chromatography on silica gel (eluent: pentane) gave a mixture of the product **22** and **7c** (350 mg) as a yellow solid. This solid was dissolved in toluene (3 mL) and the solution extracted continuously with perfluoromethylcyclohexane until the upper layer was colorless. Concentration of the toluene layer then gave pure **22** as a white solid. M.p. 77-79 °C; (250 mg, 97%). ^{1}H-NMR δ: 0.29 (dd, J = 9.2, 4.8 Hz, 1H), 0.40 (t, J = 4.8 Hz, 1H), 0.49 (d, J = 13.6 Hz, 1H), 0.66 (s, 3H), 0.85-1.99 (m, 40H), 3.61 (dd, J = 10.6, 8.1 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H); ^{13}C-NMR δ: 12.0, 18.3, 18.8, 21.4, 21.6, 22.7, 22.9, 23.9, 24.4, 24.5, 27.2, 28.2, 28.4, 30.4, 30.6, 30.8, 33.2, 34.9, 35.86, 35.91, 36.3, 38.7, 39.7, 40.2, 42.5, 46.2, 56.3, 56.6, 105-120 (m), 127.0, 127.3, 132.6, 137.2; ^{19}F-NMR δ: -53.7 (m), -50.4, -49.4 (m), -49.0, -38.2 (m), -8.37 (m); ^{77}Se-NMR δ: 452.5. Anal. Calcd. for $C_{40}H_{51}F_{13}Se$: C, 56.01, H, 5.99; Found: C, 56.01, H, 5.90.

Reaction of 22 with Tris[3-(2-methoxyethoxy)propyl]stannane and 7c. A mixture of **7c** (190 mg, 0.21mmol), **22** (17.2 mg, 0.02 mmol), tris[3-(2-methoxyethoxy)propyl]-stannane[36,37] (100 μL, 0.25 mmol) and AIBN (1 mg, 0.004 mmol) in benzene (0.2 mL) was stirred at room temperature for 30 min under Ar.

The resulting clear solution was irradiated analogously to **8**. **7c** was recovered by fluorous extraction in the jacketed continuous extractor (185 mg, 97%). Column chromatography of the non-fluorous layer on silica gel (eluent: pentane) gave a mixture of reduction product **23**[38] and rearrangement product **24**[39] as in the ratio of 58: 42 (5mg, 65%).

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