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Selenium catalysed oxidations with aqueous hydrogen peroxide. Part 3: Oxidation of carbonyl compounds under mono/bi/triphasic conditions

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Abstract—The total synthesis of 3,5-bis(perfluorooctyl)phenyl butylselenide (**1**), a recyclable catalyst for oxidation reactions with hydrogen peroxide, is described. The catalyst can be used for oxidation of aldehydes and ketones under monophasic, but also fluorous biphasic or fluorous triphasic conditions.

1. Introduction

To most chemists, selenium is not the most popular element of the periodic table. Organoselenium compounds have a reputation of being malodorous, toxic and sometimes unstable, readily producing amorphous selenium red.[1] Until the early 1970s only SeO_2 (in, for instance, allylic oxidations)[2,3] and Se (as a dehydrogenating agent) were used. However, following the discovery of *syn*-selenoxide elimination,[4] selenium compounds started to play an important role in organic chemistry, judging from the numerous review articles that have appeared over the years.[5]

Soon after the discovery of *syn*-selenoxide elimination Barton and Ley popularised the synthetic utility of benzeneseleninic acid and benzeneseleninic anhydride as stoichiometric oxidants.[6] In the mid 1970s, Sharpless found that arylseleninic acids are good oxidation catalysts in combination with TBHP[7] and aqueous hydrogen peroxide,[8] thus extending their usefulness. A further improvement in the field of selenium catalysed oxidations came with the introduction of electron-withdrawing nitro[8–10] and trifluoromethyl[11,12] substituents on the aromatic ring, making the catalysts more selective.

Arylseleninic acids (**2**) catalyse oxidations with hydrogen peroxide via the formation of the corresponding perseleninic acid (**3**), which is the active oxidant (see Fig. 1).

The arylseleninic acids can be generated in situ by reaction of the corresponding diaryldiselenide (**4**) or alkylarylselenide (**5**) with hydrogen peroxide (see Fig. 2).

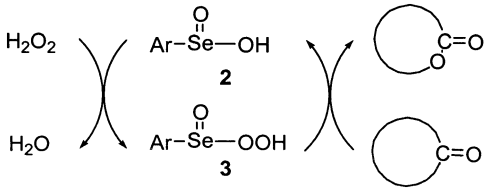

Figure 1. Oxidation of carbonyl compounds with H_2O_2 catalysed by arylseleninic acids.

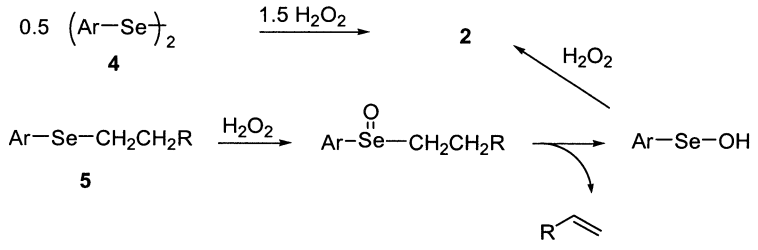

Figure 2. Formation of arylseleninic acids.

Keywords: selenium; oxidation; hydrogen peroxide; Baeyer–Villiger; fluorous phase.
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Nowadays, many different types of oxidation reactions catalysed by selenium compounds are known, such as: epoxidation of olefins;[11] allylic oxidation of olefins;[2b] Baeyer–Villiger oxidation;[9,12,13] oxidative ring contraction of cycloalkanones,[14] oxidation of sulfides to sulfoxides[15,16] or sulfones;[10] oxidation of amines to hydroxylamines, imines (to give ketones), nitro-compounds, nitrones,[17] or nitroxides;[18] oxidation of hydrazones to e.g. cyanides;[19] oxidation of aldoximes to esters;[20] oxidation of other heteroatoms such as Se,[21] As, P,[22] Si, etc. to their oxides; oxidation of alcohols to aldehydes and ketones, etc.[23,24]

Herein we report the synthesis of a recyclable selenium catalyst that can be used under monophasic, biphasic or triphasic conditions. The activity and 'recyclability' of the catalyst is demonstrated in the oxidation of aldehydes and ketones.

1.1. Toxicity of selenium compounds

One drawback of the versatile selenium catalysts is their reputed toxicity.[25,26] This requires a more precise delineation, however. The toxicity of selenium compounds depends partly on their respective oxidation states. These are: −2 (in e.g. diorganoselenides and 'seleno'-aminoacids such as selenomethionine, selenocysteine); 0 (elemental Se and selenodiglutathione); +4 (in SeO_2 and seleninic acids: RSe(O)OH) and +6 (in selenic acids: $RSe(O)_2OH$). Among the most toxic are sodium selenite, sodium selenate, selenomethionine and selenoglutathione with LD_{50} comparable to that of KCN (LD_{50}~10 mg/kg). It should be noted, however, that a daily intake of up to 0.75 mg selenium does not lead to any adverse effects[†] and that selenium is an essential micronutrient.

2. Results and discussion

2.1. Total synthesis of 3,5-bis(perfluorooctyl)phenyl butylselenide

To avoid contamination of products with selenium catalysts, the latter have been immobilised on a solid (polystyrene) support[27] and in a fluorous phase[28,29] (see Fig. 3).

Following our discovery that bis[3,5-bis(trifluoromethyl)-phenyl] diselenide (**6a**, see Fig. 4) was a significantly better oxidation catalyst than the bis[2,4-bis(trifluoromethyl)-phenyl] diselenide isomer,[11,12] we attempted to synthesise

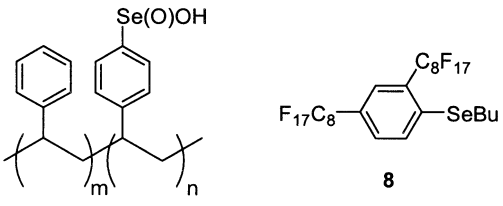

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Figure 3. Immobilised selenium catalysts.

[†] Compare: in catalytic experiments circa 10^{-2} mmol (0.8 mg) of selenium was used.

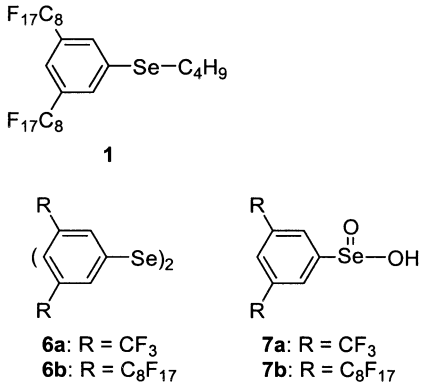


Figure 4. 3,5-Disubstituted arylselenium compounds.

the perfluoro-analogue of the former: bis[3,5-bis(perfluorooctyl)phenyl] diselenide (**6b**).

This catalyst, however, proved to be difficult to prepare and to handle. Therefore, 3,5-bis(perfluorooctyl)phenyl butylselenide (**1**) was chosen as a more suitable precursor of the same active species: 3,5-bis(perfluorooctyl)benzeneseleninic acid (**7b**). The total synthesis of selenide **1** (see Fig. 5) is largely analogous to that of 2,4-bis(perfluorooctyl)phenyl butylselenide (**8**, see Fig. 3) reported by Knochel.[28] The active catalysts derived from both isomeric catalysts have circa 63 wt% fluorine in the molecule.[‡]

As the aromatic ring is substituted in the 1,3,5-positions, the intermediate 3,5-diiodoaniline (**9**) cannot be made via direct iodination of an aniline derivative, because of the *o*,*p*-directing properties of the amino substituent. Therefore, the starting compound in the total synthesis was *p*-nitroaniline (see Fig. 5).

This aniline was iodinated with ICl[30]—a more electrophilic reagent than I_2 itself. The amino group was solely used to direct the iodination and was removed afterwards via diazotisation and reduction in alcohol.[31] The 3,5-diiodonitrobenzene thus obtained was reduced slightly below room temperature with H_2/Raney Ni to give aniline **9** analogous to the reduction of 3,5-dibromonitrobenzene.[32] Copper bronze coupled 2 equiv. of perfluorooctyl iodide with this unprotected amine **9** to yield the 3,5-bis(perfluorooctyl)aniline (**10**). The fluorous ponytails introduced at this point have a large influence on the behaviour of the products. Therefore, the number of reaction steps should be minimised from here on. In this light, synthesis of 3,5-diiodo-1-selenocyanatobenzene via diazotisation of aniline **9** (reaction 1, Fig. 6) and coupling of this product with the perfluorooctyl tails was tried. This strategy failed, however: diazotisation of aniline **9** gave an unstable intermediate that exploded violently on drying. Although some 3,5-diiodo-1-selenocyanatobenzene could be obtained from the residue, this is clearly not a practical route. Diazotisation of the 3,5-bis(perfluorooctyl)aniline to the iodide was successful,

[‡] A 60–65 wt% fluorine is a prerequisite for effective solubilisation in the fluorous phase after phase separation. Note that these two compounds have no spacer groups between the aromatic ring and fluorous ponytail. Often, a C2 or C3 spacer is used to minimise electronic effects of the 'perfluorotail' on the aromatic ring.

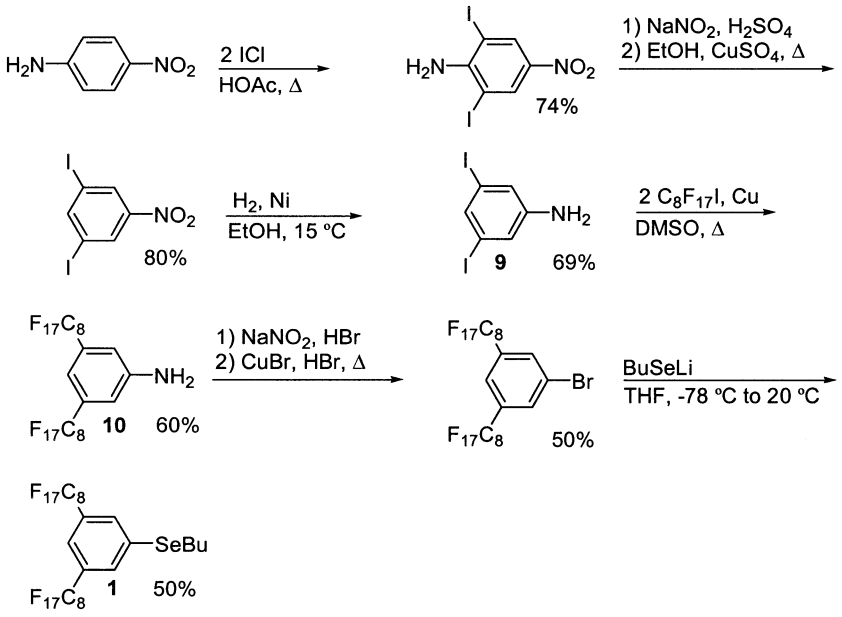


Figure 5. Total synthesis of selenide **1**.

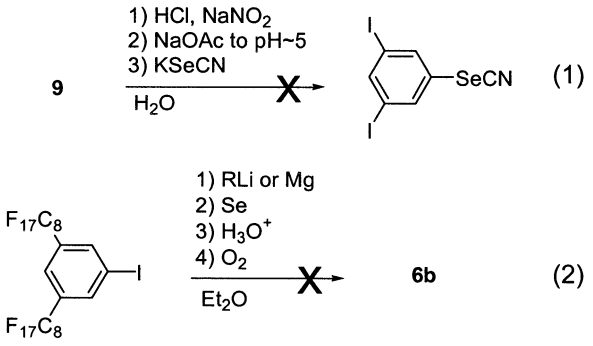


Figure 6. Unsuccessful reactions in the synthesis of **1**.

albeit in low yield. This compound, however, did not react with magnesium, *n*-BuLi, *sec*-BuLi, or *tert*-BuLi in order to obtain an organomagnesium or -lithium compound that would react with elemental selenium (reaction 2, Fig. 6). The only fruitful way found to synthesise an aryl selenium compound soluble in fluorous phase was via nucleophilic substitution of the 3,5-bis(perfluorooctyl)-1-bromobenzene—also obtained via diazotisation of the analogous aniline **10**—with lithium *n*-butylselenide. The overall yield after 6 steps was circa 6%. This can presumably be improved by further optimisation of reaction conditions.

2.2. Oxidation reactions catalysed by 3,5-bis(perfluorooctyl)phenyl butylselenide

2.2.1. Catalysis under monophasic conditions. The activities of 3,5-bis(trifluoromethyl) benzeneseleninic acid (**7a**) and 3,5-bis(perfluorooctyl)benzeneseleninic acid (**7b**)—generated in situ from diselenide **6a** and selenide **1**, respectively—were compared in the Baeyer–Villiger oxidation[33] of cyclopentanone in 1,1,1,3,3,3-hexafluoro-2-propanol at 20°C (Fig. 7). This solvent was chosen because it dissolved hydrogen peroxide, the substrate and both catalysts. Under these monophasic conditions the seleninic acid **7a** gave an initial turnover frequency (TOF) of ca. 45 h^{-1} and complete conversion in 4 h (Fig. 8). The seleninic acid **7b**, on the other hand, gave an initial TOF of ca. 75 h^{-1} and complete conversion was reached in 2 h. We attribute the higher activity of the perfluorooctyl derivative to the stronger electron-withdrawing properties of the perfluorooctyl compared to the trifluoromethyl substituents. Having confirmed that the 3,5-bis(perfluorooctyl)-benzeneseleninic acid is active in Baeyer–Villiger oxidations, we proceeded to test this catalyst under fluorous biphasic and triphasic conditions.

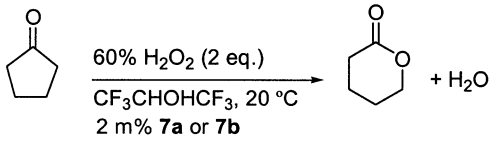


Figure 7. Baeyer–Villiger oxidation of cyclopentanone.

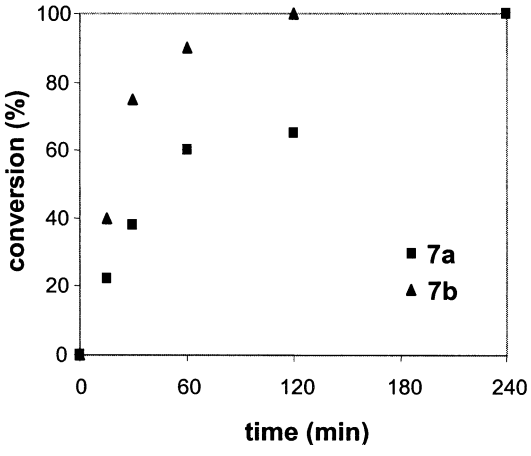


Figure 8. Conversion of cyclopentanone in time.

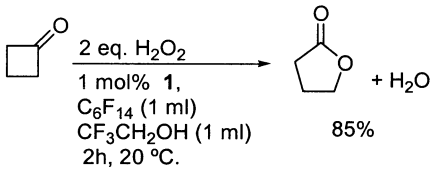


Figure 9. Oxidation of cyclobutanone under fluorous biphasic conditions.

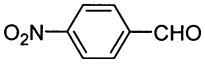
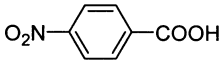
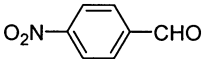
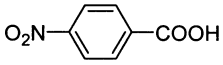
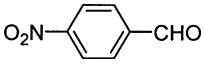
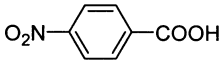
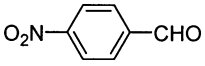
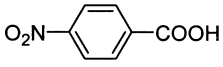
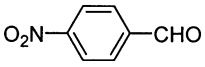
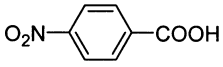
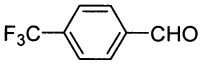
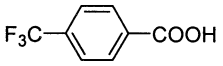
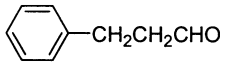
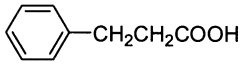
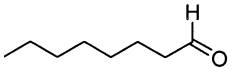
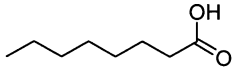
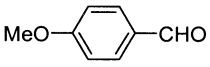
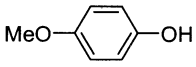
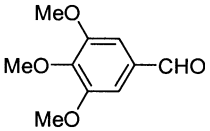
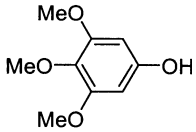
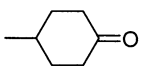
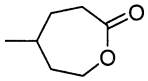
2.2.2. Catalysis under biphasic conditions. A biphasic system was obtained with a mixture of perfluorohexanes (a mixture of C_6F_{14} isomers) or perfluorodecalin containing the catalyst and 2,2,2-trifluoroethanol containing hydrogen peroxide. 2,2,2-Trifluoroethanol is known to be responsible for high activity in epoxidation and Baeyer–Villiger reactions[34] and is therefore an interesting candidate for a co-solvent. The catalyst precursor **1** was readily soluble in perfluorohexanes. However, after oxidation of the seleno-ether to the (per)seleninic acid with aqueous hydrogen peroxide, the surfactant-like structure of the (active) catalyst caused problems. Analogous to findings of Knochel[28] we observed formation of an emulsion when the active (per)-seleninic catalyst in a perfluorinated solvent came into contact with aqueous hydrogen peroxide. Especially with 2,2,2-trifluoroethanol as a co-solvent the tendency to form emulsions was strong. After reaction the two phases separated only after several hours, but, surprisingly, only a small amount of catalyst was present in the 2,2,2-trifluoroethanol layer. The partition coefficient of the perseleninic acid catalyst in perfluorohexanes/2,2,2-trifluoroethanol at 20°C is ~10. It should be noted that the reaction can be carried out at low temperatures, which may be especially useful when substrates or products are involved that are sensitive to high temperatures or that have low boiling points.

A typical reaction that may be carried out with this system is the oxidation of cyclobutanone (bp 99°C) to the moderately sensitive γ-butyrolactone (see Fig. 9).

The catalyst was very effective in the oxidation of cyclobutanone, and the reaction mixture had to be cooled with a water bath. Within 2 h conversion was complete. The product γ-butyrolactone was obtained in 85% isolated yield.

2.2.3. Catalysis under triphasic conditions. Other solvents that can be used as a second organic phase—miscible with product, non-oxidisable, polar, non-basic—are scarce. With the additional requirement that the organic solvent must be

Table 1. Oxidation of carbonyl compounds under triphasic conditions

Substrate	Product	Cycle	Isolated yield (%)
		1	90
		2	71
		3	86
		4	78
		5	50
		–	90
		–	75
		–	80
		–	70
		–	75
		–	80

Conditions: 0.04 mmol **1** (2 mol%), 2 mmol substrate, 4 mmol 60% H_2O_2, 1 ml perfluorodecalin, 1 ml 1,2-dichloroethane, 4–8 h, 80°C.

poorly miscible with a perfluorinated solvent (at low temperatures), this leaves indeed very few potential candidates. Toluene, for instance, would qualify, but suffers from side-chain oxidation. Other aromatic solvents, such as benzene, fluorobenzene or chlorobenzene, may meet the requirements above, but are often rather toxic. We note that 1,2-dichloroethane is also not ideal in this respect, but it is a very good solvent for many oxidation reactions, and it is easily removed from the product due to its relatively low boiling point. When substrates and products are not very sensitive toward overoxidation, hydrolysis, etc., good activity can be obtained at elevated temperatures with 1,2-dichloroethane as the second organic phase. Table 1 shows a range of substrates that was oxidised under fluorous triphasic conditions. Importantly, formation of emulsions in this triphasic system was strongly reduced, and the catalyst was not extracted to a large extent. The partition coefficient of the perseleninic acid catalyst in perfluorohexanes/1,2-dichloroethane at 20°C is >100, comparable to the value obtained by Knochel.[28]

The triphasic system allowed facile separation and recycling of the catalyst phase. The activity of the catalyst decreased slightly in the oxidation of *p*-nitrobenzaldehyde after several recycling experiments due to mechanical loss of the catalyst and possibly due to decomposition. The electron-poor benzaldehydes and aliphatic aldehydes showed preferential hydrogen migration to give benzoic acids and alkanoic acids, respectively. The electron-rich *p*-anisaldehyde and 3,4,5-trimethoxybenzaldehyde gave facile migration of the phenyl group to yield the formate esters of the respective phenols. These hydrolysed under the reaction conditions, however, and only phenols were obtained. Lastly, 4-methylcyclohexanone was oxidised to the lactone. In all these cases extraction of the catalyst to the organic (1,2-dichloroethane) phase was negligible.

3. Conclusions

3,5-Bis(perfluorooctyl)benzeneseleninic acid is a highly active catalyst for oxidation of aldehydes and ketones with aqueous hydrogen peroxide. Depending on the nature of the (second) organic solvent the catalyst can be used to oxidise substrates under monophasic but also fluorous biphasic or triphasic conditions.

4. Experimental

4.1. Catalytic reactions in 1,1,1,3,3,3-hexafluoro-2-propanol

Hydrogen peroxide (60%, 4 mmol, 200 μl) was added to a stirred solution (1000 rpm) of the appropriate amount of catalyst (**1** or **6a**, 2 mol% on active 'Se') in 1,1,1,3,3,3-hexafluoro-2-propanol (2 ml) in a closed flask. After the solution had become colourless, dibutyl ether (0.4 mmol, 67 μl) as internal standard and cyclopentanone (2 mmol, 178 μl) were added. The reaction temperature was kept at 20±1°C with a water bath. Samples (~50 μl) were first treated with MnO_2 (10 mg)+$MgSO_4$ in Et_2O (2 ml) and subsequently filtered and analysed with GC. Identities of the products were confirmed by GC/MS.

4.2. Catalytic reactions in perfluorohexanes/2,2,2-trifluoroethanol

Hydrogen peroxide (60%, 4 mmol, 200 μl) was added to a stirred solution (1000 rpm) of 3,5-bis(perfluorooctyl)phenyl butylselenide (0.02 mmol, 20 mg) in perfluorohexanes (1 ml) and 2,2,2-trifluoroethanol (1 ml). The mixture was stirred at room temperature for 1 h and cyclobutanone (2.0 mmol, 140 mg, 150 μl) was added. After reaction dichloromethane (5 ml) was added, the mixture was cooled to 0°C. The product phase (top) was separated, diluted with ether (5 ml), treated with MnO_2 and dried over $MgSO_4$. The salts were filtered off, the solvent was removed under reduced pressure. Yield=150 mg, ~1.7 mmol, ~85% of γ-butyrolactone.

4.3. Catalytic reactions in perfluorodecalin/1,2-dichloroethane

Hydrogen peroxide (60%, 4 mmol, 200 μl) was added to a stirred solution (1000 rpm) of 3,5-bis(perfluorooctyl)phenyl butylselenide (0.04 mmol, 40 mg) in perfluorodecalin (1 ml) and 1,2-dichloroethane (1 ml). The mixture was heated to 80°C and stirred for 1 h to form the active catalyst. After the substrate was added the reaction was stirred for the indicated period of time. With aromatic substrates the course of the reaction was followed by TLC (5% MeOH/CH_2Cl_2). After reaction the mixture was cooled to 10°C, the product phase was separated, diluted with ether (~10 ml, more in case of *p*-nitrobenzoic acid: product was poorly soluble) treated with MnO_2 and dried over $MgSO_4$. After filtration of the salts the product was purified via crystallisation or silica gel chromatography.

4.4. Syntheses

4.4.1. 2,6-Diiodo-4-nitroaniline. The compound was synthesised as described in literature.[30,35] Yield=58 g (149 mmol, 74%, lit.: 56–64[30] and 86%[35]) of a yellow solid. Mp=246–248°C (lit.:[35] 249–250°C); ^{1}H NMR (300 MHz; DMSO-d6) δ 8.44 (2H, s, 2ArH), 6.38 (2H, s, NH_2); ^{13}C NMR (75 MHz; DMSO-d6) δ 153.7 (C4), 138.2 (C1), 135.3 (C3+C5), 79.0 (C2+C6).

4.4.2. 3,5-Diiodonitrobenzene. Concentrated H_2SO_4 (96%, 15 ml) was cooled to 0°C and 2,6-diiodo-4-nitroaniline (10 mmol, 3.9 g) was added in small portions. After the aniline had dissolved an excess of $NaNO_2$ (22 mmol, 1.5 g) was added at 0°C and the mixture was left to stand for 2 h at this temperature. The brown–purple viscous solution was poured on ice (100 g) and any solid material was filtered off. The yellow filtrate was carefully poured in a large volume of boiling EtOH (100%, 200 ml) containing $CuSO_4{\cdot}5H_2O$ (1 mmol) to reduce the diazonium salt. Reduction with $CuSO_4$,[31] worked better than with metallic copper.[36] After cooling to room temperature, solid 3,5-diiodonitrobenzene separated. The product was filtered off and washed with water until neutral. The product was crystallised from EtOH (~15 ml solvent/g) to give fine brown needles. Yield=3.2 g (~85%, product was

contaminated with a trace of 3-chloro-5-iodonitrobenzene). Mp 103°C (lit.:[37] 103.5°C); ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.51 (2H, d, J=1.5 Hz, H2+H6), 8.37 (1H, d, J=1.5 Hz, H4); ^{13}C NMR (75 MHz; $CDCl_3$) δ 151.0 (C4), 148.5 (C1), 131.8 (C2+C6), 94.1 (C3+C5); MS (EI) m/z 375 (100), 329 (44, M−NO_2), 202 (31, M−NO_2–I), 127 (11), 75 (81), 74 (50).

4.4.3. 3-Chloro-5-iodonitrobenzene. MS (EI) m/z 283 (100), 237 (58, M−NO_2), 225 (12), 127 (8), 126 (11), 110 (50, C_6H_3Cl), 75 (48).

4.4.4. 3,5-Diiodoaniline.[32] A solution of 3,5-diiodonitrobenzene (80 mmol, 30 g) in EtOH (100%, 150 ml) was reduced with Raney Ni (0.5 g)/H_2 (1 bar) at 15°C. After 4 h the stirring was stopped and the supernatant was poured over a filter. Enough water (ca. 200 ml) was added to the filtrate to precipitate an off-white flocculent solid. The solid was filtered off, dissolved in ether, water was separated and the organic phase was dried over $MgSO_4$. The salt was filtered of and the filtrate evaporated to dryness. The aniline was crystallised from n-pentane/EtOH (9:1) to give white needles of 3,5-diiodoaniline contaminated with a trace of 3-chloro-5-iodoaniline. Yield=18.8 g (54.5 mmol, 68%). Mp=102°C (lit.:[38] 105°C); ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.39 (1H, t, J=1.4 Hz, H4), 6.98 (2H, d, J=1.4 Hz, H2+H6), 3.6 (2H, s broad, NH_2); ^{13}C NMR (100 MHz; $CDCl_3$) δ 148.6 (C1), 134.9 (C4), 123.0 (C2+C6), 95.1 (C3+C5); MS (EI) m/z 345 (100), 218 (41, M−I), 191 (6), 172 (7), 127 (14), 91 (41, $C_6H_3NH_2$), 63 (27).

4.4.5. 3-Chloro-5-iodoaniline. MS (EI) m/z 253 (100), 126 (57, M−I), 99 (24), 90 (27), 63 (30).

4.4.6. 3,5-Bis(perfluorooctyl)aniline. A mixture of 3,5-diiodoaniline (20 mmol, 6.9 g), copper bronze (100 mmol, 6.4 g) and perfluorooctyliodide (44 mmol, 24 g, 12.0 ml) in anhydrous DMSO (60 ml) was stirred for 16 h at 125°C under N_2. After cooling copper was filtered off and washed with ether (200 ml). The filtrate was extracted with water to remove DMSO and the organic phase was dried over $MgSO_4$. The salt was filtered off, and the filtrate was evaporated in vacuo to leave a red syrup. The residue was crystallised from CH_2Cl_2 (100 ml) to give 10.9 g (11 mmol, 59%) of a white wax-like solid. Mp=60–61°C; ^{1}H NMR (400 MHz; C_6F_6) δ 7.30 (1H, s, H4), 7.20 (2H, s, H2+H6), 4.39 (2H, s, NH_2); ^{13}C NMR (100 MHz; C_6F_6) δ 150.6 (C1), 134.1 (t, C3+C5), 117.9 (2C, s, C2+C6), 117.2 (C4), 122–110 (CF_2); ^{19}F NMR (376.3 MHz; C_6F_6) δ −81.0 (6F, t, J=9.9 Hz, 2CF_3), −110.9 (4F, t, J=15.3 Hz, 2CF_2), −120.5 (2CF_2), −121.4 (4CF_2), −121.7 (2CF_2), −122.2 (2CF_2), −125.7 (2CF_2); MS (EI) m/z 929 (100), 910 (53, M−F), 560 (72, M−C_7F_{15}), 222 (10), 191 (12), 69 (15).

4.4.7. 3,5-Bis(perfluorooctyl)-1-bromobenzene. A suspension of 3,5-bis(perfluorooctyl)aniline (5 mmol, 4.65 g) in concentrated HBr (48%, 30 ml) was cooled to 5°C and a solution of $NaNO_2$ (5.5 mmol, 0.38 g) in water (1 ml) was added drop wise. The mixture was stirred for 1 h at 5°C and then poured in boiling concentrated HBr (48%, 20 ml) containing CuBr (6 mmol, 0.86 g). The mixture was stirred for 2 h at 125°C, cooled and diluted with water. The solid was filtered off, washed with water (10 ml), 10% $NaHCO_3$ (10 ml), 10% $NaHSO_3$ (10 ml) and water (10 ml). The product was crystallised from acetone and washed with n-pentane to give light yellow fine needles. Yield=2.09 g (2.1 mmol, 42%). Mp=82.5–83.5°C; ^{1}H NMR (400 MHz; $CDCl_3/C_6F_6$) δ 8.01 (2H, s, H2+H6), 7.82 (1H, s, H4); ^{13}C NMR (100 MHz; $CDCl_3/C_6F_6$) δ 140.4–140 (m, C2+C6), 137.9–137.4 (m, C4), 134.4 (t, C1), 132.7 (t, C3+C5); ^{19}F NMR (376.3 MHz; $CDCl_3/C_6F_6$) δ −81.3 (6F, t, J=9.2 Hz, 2CF_3), −111.5 (4F, t, J=15.3 Hz, 2CF_2), −121.3 (2CF_2), −122.0 (6CF_2), −122.9 (2CF_2), −126.4 (2CF_2); MS (EI) m/z 994 (20), 975 (16, M−F), 675 (6), 625 (100), 546 (11), 284 (6), 131 (13), 69 (32).

4.4.8. 3,5-Bis(perfluorooctyl)phenyl butylselenide. A suspension of Se (40 mmol, 3.2 g) in THF was cooled to −20°C and 1.6 M BuLi in hexane (40 mmol, 25 ml) was added. The solution turned from black to light red within minutes. This cold solution of BuSeLi was added to a solution of 3,5-bis(perfluorooctyl)-1-bromobenzene (5 mmol, 5.0 g) in anhydrous THF (75 ml) at −75°C and allowed to warm-up to room temperature overnight. The reaction mixture was poured in water (100 ml) and acidified with 1 M HCl. The solution was extracted with ether (4×50 ml). The organic phase was washed with 10% $NaHCO_3$ (50 ml) and water (50 ml) and dried over $MgSO_4$. The solid was filtered off, the filtrate evaporated in vacuo and the brown residue was dissolved in perfluorohexanes (5 ml). This solution was extracted with CH_2Cl_2 (5 ml) to remove Bu_2Se_2. After evaporation of the perfluorohexanes the product was crystallised from acetone. Yield=2.6 g (2.5 mmol, 50%) of an off-white solid. Mp=56–57°C; ^{1}H NMR (300 MHz; $CDCl_3$) δ 7.84 (2H, s, H2+H6), 7.61 (1H, s, H4), 3.01 (2H, t, J=7.3 Hz, $SeCH_2$), 1.71 (2H, m, $SeCH_2CH_2$), 1.45 (2H, m, CH_2CH_3), 0.92 (3H, t, J=7.3 Hz, CH_3); ^{13}C NMR (75 MHz; $CDCl_3$) δ 134.0 (C1), 133.1 (C2+C6), 130.4 (2C, t, J=24.8 Hz, C3+C5), 123.3 (C4), 31.8 ($SeCH_2$), 28.0 ($SeCH_2CH_2$), 22.8 (CH_2CH_3), 13.4 (CH_3); ^{19}F NMR (282 MHz; $CDCl_3$) δ −81.3 (6F, t, J=9.8 Hz, 2CF_3), −111.7 (4F, t, J=14.0 Hz, 2CF_2), −121.4 (2CF_2), −122.4 (6CF_2), −123.2 (2CF_2), −126.7 (2CF_2); MS (EI) m/z 1050 (63), 994 (30), 625 (17, M−C_4H_9−C_7F_{15}), 545 (12, $C_6H_3(CF_2)C_8F_{15}$), 131 (12), 57 (C_4H_9, 100).

4.5. Materials

Bis[3,5-bis(trifluoromethyl)phenyl] diselenide was prepared via reaction of 3,5-bis(trifluoromethyl)phenylmagnesium bromide with elemental selenium and subsequent aerobic oxidation of the corresponding benzeneselenol.[11] Glacial acetic acid, n-BuLi (1.6 M in hexane), perfluorohexanes (FC 72), perfluorodecalin (95%), cyclobutanone (98+%), cyclopentanone (99+%) 3-phenylpropanal (97%), octanal (99%), 3,4,5-trimethoxybenzaldehyde (99%), 4-nitrobenzaldehyde (99%) and 4-(trifluoromethyl)benzaldehyde (95%) were purchased from Acros. Anhydrous THF (99.5+%), ICl (97%), perfluorooctyl iodide (98+%), 2,2,2-trifluoroethanol (99+%) and 1,1,1,3,3,3-hexafluoro-2-propanol (99+%) were purchased from Fluka; 1,2-dichloroethane (99+%), 48% HBr and 96% H_2SO_4 from Baker; copper powder (99%) and p-anisaldehyde (98+%) from Aldrich; elemental Se (99+%) from Merck; CuBr

from Riedel; *p*-nitroaniline (97%) from BDH Chemicals Ltd; $CuSO_4 \cdot 5H_2O$ (98.7%) from Lamers and Pleuger B.V.; DMSO (99.7%) from Acros was dried on mol sieves 3 Å. Hydrogen gas from Air Products. Raney Ni (B115Z) was a gift from Degussa; hydrogen peroxide (60%) was a gift from Solvay Interox.

4.6. Analyses

Melting points were determined with a Buchi 510 Melting Point Apparatus with open capillary. GC measurements were carried out with a Varian Star 3400 equipped with a CP Sil 5-CB column (50 m×0.53 mm). ^{1}H, ^{13}C and ^{19}F NMR spectra were carried out on a Bruker AC 300 or Varian VXR 400S spectrometer. Chemical shifts (δ) relative to tetramethylsilane (TMS). Gas chromatography/mass spectrometry (GC/MS) analyses were performed on a VG 70-SE mass spectrometer equipped with a CP Sil 5-CB column.

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