Studies on Substituted Aromatic Diselenides as Catalysts for Selective Alcohol Oxidation Using *tert*-Butyl Hydroperoxide

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We have investigated the Ph_2Se_2 -catalysed oxidation of alcohols with *tert*-butyl hydroperoxide (TBHP) by using a variety of spectroscopic techniques and reaction calorimetry. We showed that the active oxidant is benzeneseleninic anhydride (BSA), formed by reaction of Ph_2Se_2 with TBHP. The influence of aromatic substituents on the activity of a selection of nine aromatic diselenides involved in alcohol oxidations was studied. Calorimetric experiments showed that compounds that are activated more rapidly have higher initial activity in the catalytic oxidation of benzyl alcohol. An

Introduction

The selective oxidation of alcohols is a prominent transformation in organic chemistry, and there is an ongoing quest for selective and sustainable methods.^[1] The use of aromatic diselenide-based oxidation catalysts was first reported in 1978,^[2] and these reagents have subsequently been shown to be versatile and selective catalysts in a number of oxidative transformations.^[3] Among other reactions, they catalyze the oxidation of alcohols, albeit with generally high catalyst loadings (Figure 1). Many groups have reported the use of different diselenides in alcohol oxidations.[4-7] However, a systematic investigation of different diselenides in combination with an easily accessible oxidant has not been published. One of the best selenium catalysts in terms of substrate scope is dimesityl diselenide, although the catalyst loading is usually 50 mol-%.^[4] Kuwajima and co-workers reported the effective use of bis(p-chlorophenyl) diselenide



Figure 1. Catalytic oxidation of alcohols with aromatic diselenides.

exception to this rule was observed when the diselenide contained a dimethylamino group in the *ortho* position, which can apparently compensate for its slow pre-activation by a special *ortho* effect. An aliphatic alcohol, 1-decanol was also used as a substrate. Besides diphenyl diselenide only three of the substituted diaryl diselenides studied showed reasonable activity after pre-activation with TBHP. Dimesityl diselenide displayed the highest activity and selectivity for the oxidation of 1-decanol. Specificity for a given aldehyde could be achieved by using an oxidant and substrate feed protocol.

in the oxidation of the allylic alcohol (*E*)-2-hexen-1-ol with TBHP, although the catalyst loading was not reported.^[5]

Using *N*-chlorosulfonamides, such as Chloramine-T sodium salt or *N*,4-dichlorobenzenesulfonamide sodium salt, Kuwajima and co-workers observed a large improvement with diphenyl diselenides containing ketone or ester groups as *ortho* substituents on the catalysts in the oxidation of activated alcohols. In a more recent article, bis[2-(2-pyridyl)phenyl] diselenide was shown to be a more efficient catalyst in combination with an *N*-chlorosulfonamide as the oxidant, and catalyst loadings could be reduced to 0.2 mol- $%.^{[7]}$ These findings demonstrate that aromatic diselenides still hold great promise for catalytic oxidations of alcohols.

Recently, we revisited the oxidation of alcohols using Ph_2Se_2 as the catalyst and TBHP as the terminal oxidant. Results of a mechanistic study indicated the involvement of an autocatalytic step with benzeneseleninic anhydride (BSA) as the key intermediate (Figure 2). Based on these results we were able to develop a procedure for the catalytic oxidation of activated alcohols using TBHP and 1 mol-% of Ph_2Se_2 as catalyst.^[8] The formation of BSA was monitored by using reaction calorimetry in the absence of the alcohol substrate. Its formation exhibited a distinct exothermic profile, which we attributed to some sort of autocatalysis. Driven by the potential of diselenides as catalysts, there is a need to gain deeper insight in the mechanism of the reaction.

Our first goal in the present study was to further extend our knowledge of how Ph_2Se_2 is activated by TBHP at elevated temperatures. To accomplish this goal a range of spectroscopic techniques was applied (Step 1). Our second goal

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Figure 2. Catalytic cycle of the diselenide-catalyzed oxidation of alcohols.

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was to investigate the influence of various substituents on the pre-activation of substituted diselenides. The potential of these compounds as catalysts in the oxidation of alcohols, including aliphatic ones, was studied with the aim of expanding the scope of alcohol substrates amenable to oxidation.

Results and Discussion

Spectroscopic Studies of the Formation of BSA as the Active Oxidant from Diphenyl Diselenide

In our previous studies of the Ph_2Se_2 -catalyzed oxidation of benzyl alcohol we observed an induction period during which no substrate was converted. This suggested that the activation of Ph_2Se_2 needed to be complete in order for the catalytic reaction to start. When testing this hypothesis by simply mixing Ph_2Se_2 with TBHP in toluene we observed a peak in reaction calorimetry after approximately 25 min. We found that if we added the substrate after this exothermic event, conversion of the substrate was almost instantaneous. The oxidation of Ph_2Se_2 to BSA (Figure 2, Step 1) consists of three two-electron oxidations, and several possible pathways can be envisaged.

We started our study using UV/Vis spectroscopy, which is highly suitable for determining the initial oxidation as oxidized selenium species, such as diphenyl selenoxide, do not absorb light above 300 nm.^[9] Samples were withdrawn from the reaction mixture and were consecutively diluted, thus allowing for absorption measurement acquisitions (Figure 3). After mixing the warm sample with cold toluene, the signal was constant for several hours. The absorption maximum around 330 nm almost immediately decreased to one third of its original intensity upon exposure of 1 equiv. of Ph₂Se₂ to 1 equiv. of TBHP. After 10 min, no further changes in absorption could be detected. We assign the observed change in the absorption signal to the first oxidation of the diselenide. We know that, at this stage, the BSA is not yet formed since we have observed that the oxidation of benzyl alcohol does not start when added after 10 min.^[8] In contrast, if we added the benzyl alcohol after 40 min, an equimolar amount was oxidized (95% yield).



Figure 3. Spectral changes of Ph_2Se_2 upon oxidation with TBHP and subsequent addition of benzyl alcohol (after 40 min).

To further investigate the nature of the active species, we turned to in situ Raman and IR spectroscopy. The IR data are relevant in view of the Se=O stretch vibration, which has a complicated and intense absorption around 850 cm^{-1} .^[10] The IR data corroborated previously acquired UV data as there was again a pronounced spectral change after 5 min. The time plots of two distinct selenium–oxygen vibration frequencies (860 and 840 cm⁻¹) are shown in Figures 4 and 5. From the combination of the UV and IR data we hypothesize that after 5 min the first Se=O bond is formed (Figure 4). When this process is almost complete, the second Se=O stretch appears in the spectrum (Figure 5).



Figure 4. Time profile of IR band at 860 cm⁻¹ during the activation of Ph_2Se_2 by TBHP. At t = 39 min, 1 equiv. of benzyl alcohol was added.

In Raman spectroscopy, the Se–Se stretch vibration has a distinct frequency, providing us with information on the time of the putative Se–Se bond cleavage. Unfortunately, spectra could only be recorded in heptane, which suffered a major drawback; after 23 min, BSA started to precipitate from the solution. However, the activation profile of Ph_2Se_2



Figure 5. Time profile of IR band at 840 cm⁻¹ during the activation of Ph_2Se_2 by TBHP. At t = 39 min, 1 equiv. of benzyl alcohol was added.

by TBHP in reaction calorimetry was almost identical (data not reported here). Therefore, we feel that the data obtained in either toluene or heptane are interchangeable. From our previous experiments we expected a change in composition between 10 to 15 min after addition of the TBHP. Indeed, after 15 min a large drop in the Se–Se stretch vibration was observed (Figure 6). We presume that this event is indicative of BSA formation, which corroborates the calorimetric profile showing strong exothermicity after 15 min of reaction. A tentative mechanism can be envisaged for the activation of Ph₂Se₂ (Figure 7).



Figure 6. Normalized Raman spectral data; upper line Se–Se stretch vibration (310 cm⁻¹), lower line C=O stretch vibration (1710 cm⁻¹). TBHP was added at t = 0 min and benzyl alcohol (0.9 equiv.) at t = 39 min.

The first oxidation (Ox I) of 1 to 2 is consistent with UV and IR spectral data and occurs within 5–10 min. After this, the second oxidation of 2 to 3 (Ox II) takes place as evidenced by IR spectroscopy. The final oxidation of compound 3 to BSA (4) then occurs between 15 and 20 min, as shown by Raman spectroscopy and calorimetry. In this scenario (Figure 7) we have also included the formation of species 5. In our previous study we postulated that this intermediate is most likely responsible for the autocatalysis (vide supra) that occurs when 4 is formed. *tert*-Butyl per-



Figure 7. Path of autocatalytic activation of Ph₂Se₂ by TBHP.

oxyphenylseleninate (5) is presumed to be a more effective oxygen transfer oxidant than TBHP itself. Using NMR spectroscopy, we expected to observe other oxidized selenium compounds in addition to BSA at the end of the reaction. We studied the activation of Ph_2Se_2 by 1 equiv. of TBHP using NMR spectroscopy. The time course of the aromatic region of the NMR signals is shown in Figure 8.



Figure 8. NMR spectra of the activation of Ph_2Se_2 by TBHP, data shown for the region of $\delta = 8.5-7.5$ ppm. After t = 30 min, 1 equiv. of benzyl alcohol was added.

The spectra revealed two new sets of peaks only after 15 min, which increased in intensity up to 25 min. The newly found signals correspond to BSA, in a quantity of $^{1}/_{3}$ of the mixture, while the other $^{2}/_{3}$ of the mixture was the remaining Ph₂Se₂. We were not able to find any distinct signals that could be attributed to other intermediates on the path from Ph₂Se₂ to BSA. This is consistent with a literature report on the oxidation of bis(*p*-fluorophenyl) diselenide monitored by ¹⁹F NMR spectroscopy.^[11] This is a remarkable feature of the oxidation of these two aromatic diselenides. Apparently, the second and third oxidation of Ph₂Se₂ proceeds much more easily than the first as sug-

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gested by the formation of a 2:1 mixture of Ph_2Se_2 and BSA, rather than a more complex mixture of selenides in different oxidation states.

Study of Substituted Diselenides as Pre-catalysts in Oxidations with TBHP

The influence of aromatic substituents, on the potential of diselenides as pre-catalysts in oxidations with TBHP was investigated. The goal was to extend the substrate scope of the current method towards non-activated alcohols. For this purpose a selection of substituted diaryl diselenides was tested (Figure 9).



Figure 9. Selected compounds used to investigate the substituent effect.

Compound **1** is, by definition, our reference catalyst. Compound **2** [bis(2-nitrophenyl) diselenide] is a well-known and often-applied epoxidation and Baeyer–Villiger oxidation catalyst.^[12] Compound **3** has been referred to as an effective catalyst in the oxidation of allylic alcohols.^[5] Compound **4** is known to be a very effective pre-catalyst for alcohol oxidations, although the catalyst loading is often very high.^[5] Compounds **5** and **6** were selected for comparison with compound **4**. Compounds **7** and **8**, in contrast to compound **2**, possess electron-donating groups in the *ortho* position of the aromatic ring. Bis(pentafluorophenyl) diselenide (**9**) was selected, because the corresponding seleninic acid was previously reported as an active reagent in dehydrogenations of non-activated alcohols.^[13] The commercially not available compounds, except for **9** (which was prepared by direct lithiation of pentafluorobenzene followed by reaction with selenium^[14]), were constructed by using the corresponding Grignard reagents. During these syntheses, we noticed that the Grignard reactions often led to large amounts of monoselenide adducts besides the diselenide.^[15] The only way these could be separated was by reversed-phase silica chromatography. Bis[2-(dimethylamino)phenyl] diselenide (**8**) was successfully prepared by using a Knochel Mg/Br exchange, after which point, the higher ate complex was created by adding 1 equiv. of dioxane.^[16] This complex was treated with elemental selenium to yield the target compound.

The reaction of compounds 1-9 with TBHP was studied by using calorimetry. In this way the so-called activation time – the time needed to form the anhydride as the catalytic species – and activation energy could be measured. The influence of substituents on these parameters is listed in Table 1. Notably, the diselenide concentration was lower (6.3 mM) than in previous experiments, leading to a longer induction period of 50 min instead of the aforementioned 25 min.

It turns out that Ph_2Se_2 is one of the slowest compounds to achieve activation. The fastest of the series was found to be compound **4**, although this compound delivered the lowest heat of activation among all compounds studied. Compound **8** showed the same profile as **1**, but it had the highest activation energy, more than twice that of most other diselenides. Very remarkable were the data for the series of compounds **4**–**6**; the dimesityl diselenide was faster to achieve activation than either the 4- or 3-methyl-substituted catalysts. Methylation at the 3- or 4-positions significantly slowed the oxidation.

Substituted Diaryl Diselenides in the Catalytic Oxidation of Benzyl Alcohol

Having established the activation behaviour of catalysts in the absence of substrate, the overall reaction efficiency for the catalytic oxidation of benzyl alcohol by using 5 mol-% of compounds 1-8 was studied. The results are presented in Figure 10 for the compounds with the lowest rates and in Figure 11 for compounds with the highest rates.

Table 1. Induction period (activation times) with substituted diselenides. In each reaction diselenide (0.25 mmol) was dissolved in toluene (40 mL), and TBHP (0.5 mmol) was added at 80 °C. The activation time is defined as the time intervening the addition of TBHP and acquisition of the highest peak in the exothermic profile. The activation energy is calculated by integrating the peak area.

Entry	Diselenide	Substitution pattern	Activation time [min]	Activation energy [kJ/mol]
1	1	_	50	150
2	2	2-nitro	n.d. ^[a]	n.d. ^[a]
3	3	4-chloro	52	230
4	4	2,4,6-trimethyl	22	120
5	5	4-methyl	38	150
6	6	3-methyl	42	145
7	7	2-methoxy	n.d. ^[a]	n.d. ^[a]
8	8	2-(dimethylamino)	49	345
9	9	pentafluoro	52	190

[a] n.d. = not detected.



Figure 10. Slowest profiles for the oxidation of benzyl alcohol with diselenides (5%) at 80 °C and TBHP (1.1 equiv.).



Figure 11. Fastest profiles for the oxidation of benzyl alcohol with diselenides (5%) at 80 °C and TBHP (1.1 equiv.).

We observed that the slightly electron-donating methyl groups seem to promote fast initial turnover of the substrate. All alkyl-substituted diaryl diselenides were found to be among the fastest to convert substrate. Second, the ortho position seemed to be very important as contradictory results had been obtained with diselenides substituted at this position. Compound 7, the original epoxidation catalyst, was found to possess the lowest activity. When comparing calorimetry data obtained during pre-activation studies with activity data, a clear correlation is observed between the time of activation and the initial catalytic activity of the catalyst. The two compounds that did not show activation in the calorimetric experiments (2 and 7), showed the lowest oxidation activity. The main exception was compound 8, although we hypothesize that the 2-(dimethylamino) group could possibly act as a base in reactions containing this diselenide. Calorimetry data obtained with 8 suggests that it does not have an effect on activation, but that the dimethylamino moiety may play an important role in dictating catalytic activity.

The above results demonstrate that formation of the active intermediate is highly influenced by substituents on the aromatic ring. A strong electron-withdrawing or electron-donating substituent at the *ortho* position diminishes the activity of the diselenide in catalysis. A nitrogen-con-

taining substituent on the other hand can possibly enhance the catalytic mode of action, a phenomenon that has been found in selenium-based glutathione peroxidase mimics.^[17]

Oxidation of an Aliphatic Alcohol: 1-Decanol

Previously we had shown that, using an oxidant and substrate feed in a loop cycle, high selectivity and efficiency can be attained with diphenyl diselenide as the oxidation catalyst.^[8] To further explore the scope of our substituted diselenides, a catalytic test was performed with 5 mol-% diselenide and 1-decanol as the substrate. Unfortunately, the maximum yield of decanal attained was 8%, which declined over time as it was further oxidized to capric acid. One of the other by-products was the decyl ester of capric acid.

Therefore, we decided to explore the use of an oxidant and substrate feed technique. First the capacity of different diselenides in the dehydrogenation of 1-decanol was studied in a stoichiometric fashion: pre-activation with 1 equiv. of TBHP was followed by the addition of a stoichiometric amount of 1-decanol. The conversion of substrate was monitored over time (Figure 12). In these experiments toluene was replaced by (trifluoromethyl)benzene to prevent oxidation of the solvent. Compounds **5** and **6** were not tested in these experiments because of their lack of activity in the catalytic oxidation of 1-decanol.



Figure 12. Yield of decanal at different time points with pre-activated diselenides. Diselenide (0.5 mmol) and TBHP (1.1 mmol) were premixed at 80 °C in (trifluoromethyl)benzene for 2 h, followed by the addition of 1-decanol (1 mmol).

Compounds 4, 7 and 9 all completely converted the alcohol to the aldehyde. The speed of oxidation was considerably slower than in the same experiment with Ph₂Se₂ and benzyl alcohol (the latter gave full conversion to benzaldehyde within 10 min). In the case of the oxidation of 1decanol conversion took at least 120 min. In these experiments the effect of pre-activation was excluded, and what we observed was the primary dehydrogenating activity of the corresponding selenenic anhydride with 1-decanol. It can therefore be envisaged that Step 3 in Figure 2 is favoured by strong inductive and electron-donating substituents, such as the o-methoxy group in compound 7 and the three methyl substituents in compound 4. Surprisingly, bis-(pentafluorophenyl) diselenide (9), once pre-activated, showed good activity. These results show that the actual rate-determining step during oxidation is not well under-

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stood, although we presume that a number of factors are important in the dehydrogenation of alcohols by BSA and its derivatives.

We decided to test the most promising catalysts in the batch-wise oxidation of 1-decanol, using our previously described protocol. The protocol was changed in order to prolong the period between the addition of 1-decanol and a new amount of TBHP for regeneration of the catalyst. The stepwise addition of substrate and oxidant is visualized in Figures 13 and 14.



Figure 13. Oxidation of 1-decanol with different diselenides (0.25 mmol) according to the oxidant and substrate feed protocol.



Figure 14. Capric acid formation during the oxidant and substrate feed protocol with different diselenides in the oxidation of 1-decanol. Note that the *x*-axis starts at t = 2 h.

All of the selected diselenides turned out to be good oxidation pre-catalysts by using the oxidant and substrate feed protocol. One of the main problems was over-oxidation of the product leading to capric acid, as shown in Figure 12. This reaction was also found to be selenium-catalyzed as a blank run with TBHP and 1-decanal did not show capric acid formation. The formation of intermediate perester 5 is most likely one of the main problems as this can oxidize aldehydes to the corresponding acids. In the presence of the seleninic acid, perester formation is also possible, and thus the formation of by-product cannot be suppressed. One of the main problems in this protocol is most probably the reformation of the intermediate anhydride, the active species in our reaction. It can be reasonably assumed that oxidation of benzeneselenol (the compound formed in Step 3, Figure 2) to the benzeneseleninic acid occurs rapidly. It is known that benzeneseleninic acid dehydrates to the anhydride at relatively low temperatures, typically around

70 °C.^[13] This dehydration may be more difficult for substituted diselenides, thus requiring higher temperatures. Although it is possible to heat up the mixture to higher temperatures, TBHP is unstable at temperatures above 90 °C, so this is not a viable option. However, compared to previous results in the literature, our system has the lowest catalyst loading (25%) and highest yield (98%) in the oxidation of 1-decanol.

Conclusions

We must conclude that, for the mechanism of oxidation of alcohols by substituted diselenides, there are two important parameters. First, there is the mode of activation of the diselenide by the oxidant (Figure 2, Step 1). Certain diselenides such as dimesityl diselenide (4) are easily activated by TBHP, whereas others are not activated at all. Secondly, the oxidation potential of the activated substituted diselenides differs greatly. Not all activated diselenides are capable of dehydrogenating non-activated alcohols (Figure 2, Steps 2 and 3). Finally, regeneration of the anhydride of the active species (Figure 2, Step 4) is also expected to change when the substituents are varied. The traditional catalytic oxidation of 1-decanol with aromatic diselenides was hampered by formation of side-products due to overoxidation and transesterification. However, when diselenides were first pre-activated, followed by addition of 1-decanol, compounds 4, 7 and 9 were capable of converting this substrate selectively to the aldehyde. Obviously, the steric and electronic demands for the hydrogen abstraction are optimal for these catalysts, whereas other diselenides were not capable of quantitatively converting substrate. The most promising diselenides were tested in the catalytic oxidation of 1-decanol by using our previously optimized oxidant and substrate feed protocol. It was shown that this was indeed a good way of improving catalyst performance.

We have shown that changing the electronic properties of the diphenyl diselenides provides an entry for improving their catalytic properties. However, more studies are needed in order to predict these properties and to design more active dehydrogenating selenium species.

Experimental Section

General: All reagents and solvents were used as received from their respective vendors. ¹H (400 Hz) and ¹³C (100 Hz) NMR spectra were recorded with a Bruker AC 400 spectrometer by using tetramethylsilane as an external standard. UV spectra were recorded with a UV/Vis Hewlett Packard 8452A Diode Array Spectrophotometer. Gas chromatography analysis was carried out with a Shimadzu GC2010 instrument equipped with a non-polar CP Sil-5 CB 50 m × 0.53 mm colomn by using an FID detector. Mass spectrometry data were collected with a Shimadzu GC–MS-QP2010 Ultra, equipped with a non-polar CP Sil-5 CB 50 m × 0.53 mm column. Elemental analyses were determined with a Carlo Erba Ea 1108 instrument. Melting points were recorded with a Büchi melting-point apparatus B-545.

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Spectroscopy: Reaction calorimetry was performed with a Multimax apparatus: Programmable 4 parallel reactor box, reaction volume from 25 to 70 mL with overhead stirring, temperature range from -25 to 150 °C, reflux cooler and inter-gas purging. Each reactor can be set individually for temperature and stirring. Temperature control modes: Jacket and reactor contents. Reaction calorimetry was done by adding a known amount of heat to the reaction mixture using a calibration probe, followed by integration of the signals obtained (150 Ω , 24 V). To a solution of a specific concentration of the diselenide at 80 °C was added the appropriate amount of TBHP in decane after which the temperature difference between the internal sensor (T_r ; temperature of the reaction) and the external sensor $(T_i;$ temperature of the jacket) was monitored. UV/Vis: To a heated mixture of 0.1 M Ph₂Se₂ in toluene (10 mL) was added at 80 °C an equimolar amount of TBHP in decane. After 40 min, an equimolar amount of benzyl alcohol was added to the mixture. At selected time intervals, aliquots (50 µL) were withdrawn from the reaction mixture and diluted with toluene (2.95 mL) at room temp. The UV spectrum was recorded instantly with a UV/Vis Hewlett Packard 8452A Diode Array Spectrophotometer. In situ IR spectroscopy: The IR data were recorded by using a Bruker Matrix-MF FT-IR instrument in combination with a fiber-optic diamond ATR probe. А 0.1 м solution of Ph₂Se₂ in toluene was heated to 80 °C, and TBHP (2 equiv.) in decane was added. After 40 min, benzyl alcohol (2 equiv.) was added. In situ Raman spectroscopy: The Raman data were recorded by using a Raman RXN1 analyser from Kaiser Optical systems with a standard immersion probe. A solution of Ph₂Se₂ in heptane (0.1 M) was heated to 80 °C, and TBHP (2 equiv.) in decane was added. After 40 min, benzyl alcohol (2 equiv.) was added. NMR analysis of activation of Ph₂Se₂ by TBHP: kinetic reactions were performed the same way as the UV/Vis analysis (vide supra), but the solvent for the reactions and for the dilutions was deuterated toluene.

Catalytic Oxidations: To a stirred solution of substrate (2 mmol), 1,2-dimethoxybenzene (0.5 mmol, 69 mg, internal standard) and the selected diselenide (0.1 mmol) in solvent (10 mL) was added at 80 °C TBHP (2.2 mmol). At several intervals, aliquots (50 μ L) were withdrawn, quenched with Na₂SO₃ [100 mg in EtOAc (1.5 mL)], and the solids were filtered off. The mixture was subsequently analyzed by GC.

Stoichiometric Oxidations: To a stirred solution of the diselenide (0.5 mmol), dodecane (0.25 mmol, internal standard) in (trifluoromethyl)benzene (10 mL) at 80 °C was added TBHP (1 mmol from a 5.5 M solution in decane), and after the appropriate amount of time 1-decanol (0.5 mmol) was added. At several intervals, aliquots (50 μ L) were withdrawn, quenched with Na₂SO₃ [100 mg in EtOAc (1.5 mL)], and the solids were filtered off. The mixture was subsequently analyzed by GC.

Oxidant and Substrate Feed Reactions: To a stirred solution of the diselenide (0.25 mmol), dodecane (0.25 mmol, internal standard) in (trifluoromethyl)benzene (5 mL) at 80 °C was added TBHP (0.5 mmol from a 5.5 M solution in decane), and after the appropriate amount of time 1-decanol (0.25 mmol) was added. After 2 h, 1-decanol (0.25 mmol) was added. After an additional 1 h, TBHP (0.25 mmol) was added. These steps were repeated four times. At several intervals, aliquots (50 μ L) were withdrawn, quenched with Na₂SO₃ [100 mg in EtOAc (1.5 mL)], and the solids were filtered off. The mixture was subsequently analyzed by GC.

Syntheses

Bis(4-methylphenyl) Diselenide (5): To a 1 M solution of *p*-tolylmagnesium bromide (30 mL), Se powder was added portion-wise, and after complete addition the mixture was heated to 40 °C for 30 min.

The colour of the solution changed during this time from lightbrown to bright green. After cooling the mixture to room temp., it was poured onto a mixture of ice and saturated aqueous NH_4Cl . This was stirred for 10 min, and the water layer was extracted 5 times with Et₂O. The combined organic layers were dried with MgSO₄, and the solvent was evaporated in vacuo. The residue was taken up in EtOH, and KOH (100 mg) was added. A stream of air was passed over the solution for 45 min after which the mixture was stirred in an open flask overnight. A white compound had crystallized, which was filtered off (dimer), and the mother liquor was subjected to preparative RP18 silica gel chromatography, which could separate the diselenide from the monoselenide [eluent: MeCN/H₂O (8:2), $R_f = 0.32$], which yielded a light-yellow crystalline compound. M.p. 48 °C. Yield: 879 mg, 2.57 mmol (17%). ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.48 (d, J = 6.4 Hz, 2 H), 7.07 (d, J = 7.6 Hz, 2 H), 2.34 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 138.4 (C_q), 132.7, 130.3, 128.1 (C_q), 21.5 ppm. MS: m/z = 342. $C_{14}H_{14}Se_2$ (341.94): calcd. C 49.43, H 4.15; found C 50.1, H 4.22.

Bis(3-methylphenyl) Diselenide (6): To a 1 M solution of *m*-tolylmagnesium bromide (10 mL), Se powder was added portion-wise, and after complete addition the mixture was stirred for another 3 h during which time a viscous slurry formed. The reaction mixture was poured onto a mixture of ice and saturated aqueous NH₄Cl. During this workup, large amounts of red selenium formed. This mixture was stirred for 10 min, and the water layer was extracted 5 times with Et₂O. The combined organic layers were dried with MgSO₄, and the solvent was evaporated in vacuo. The residue was subjected to RP18 silica gel chromatography which could separate the diselenide from the monoselenide [eluent: MeCN/H₂O (8:2), $R_{\rm f}$ = 0.35], which yielded a light-yellow crystalline compound. M.p. 53 °C. Yield: 366 mg, 1.07 mmol (21%). ¹H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.34 (m, 1 H), 7.25 (m, 3 H), 2.31 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 138.9 (C_q), 133.0, 129.3, 129.0, 128.7, 128.1, 21.3 ppm. MS: m/z = 342. $C_{14}H_{14}Se_2$ (341.94): calcd. C 49.43, H 4.15; found C 49.7, H 4.28.

Bis(2-methoxyphenyl) Diselenide (7): To a 1 M solution in THF of the Grignard reagent (40 mL), Se powder was added portion-wise in such a rate that the temperature did not exceed 35 °C in the reaction; 10 min after the complete addition of the Se, the mixture started to polymerize, and thus the mixture was hydrolyzed with saturated aqueous NH₄Cl. The mixture was extracted 3 times with EtOAc, the organic layers were combined, dried with MgSO₄, and subsequently the solids were filtered off. All volatiles were removed in vacuo, and the compound was purified on SiO₂ (EtOAc/hexanes, 95:5). The orange liquid was subjected to kugelrohr distillation, and two fractions were obtained, one boiling at 170 °C (0.1 mbar) and the other at 210 °C (0.1 mbar). The diselenide was recrystallized from EtOH, which yielded bright orange crystals. M.p. 79 °C Yield: 3.587 g, 9.59 mmol (48%). ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.54 (d, J = 7.6 Hz, 1 H), 7.21 (t, J = 8.0 Hz, 1 H), 6.87 (t, J = 7.2 Hz, 1 H), 6.82 (d, J = 8.0 Hz, 1 H), 3.91 (s, 3 H) ppm. ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 157.3 (C_a), 131.0, 128.6, 122.3, 119.0 (C_q), 110.6, 56.4 ppm. MS: m/z = 374. C₁₄H₁₄O₂Se₂ (373.93): calcd. C 45.18, H 3.79; found C 45.08, H 3.70.

Bis[2-(dimethylamino)phenyl] Diselenide (8): To the starting compound (5 mmol) in THF (10 mL) was added *i*PrMgCl·LiCl complex (1.1 equiv.), and after full addition dioxane (1 equiv.) was added. A precipitate was observed, and conversion of the starting material was monitored by taking samples and analysing them by GC–MS. After stirring overnight, conversion was complete, and Se

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powder was added gradually. The mixture was stirred for another 2 h and then hydrolyzed with aqueous NH₄Cl. The mixture was purified by SiO₂ chromatography (heptane) to yield a light-yellow crystalline compound. M.p. 41 °C Yield: 438 mg, 1.10 mmol (44%). ¹H NMR (400 MHz, CDCl₃, 25 °C): δ = 7.52 (d, *J* = 8.1 Hz, 1 H), 7.15 (m, 2 H), 7.00 (t, *J* = 6.4 Hz, 1 H), 2.80 (s, 6 H) ppm. ¹³C NMR (100 MHz, CDCl₃, 25 °C): δ = 152.8 (C_q), 129.3, 127.6, 126.3, 120.8, 45.8 ppm. MS: *m*/*z* = 199 [M²⁺]. C₁₆H₂₀N₂Se₂ (400.00): calcd. C 48.25, H 5.06, N 7.03; found C 48.02, H 5.11, N 7.10.

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