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Efficient trapping of the intermediates in the photooxygenation of sulfides by aryl selenides and selenoxides

Nikoletta Sofikiti, Constantinos Rabalakos and Manolis Stratakis*

Department of Chemistry, University of Crete, 71409 Iraklion, Greece

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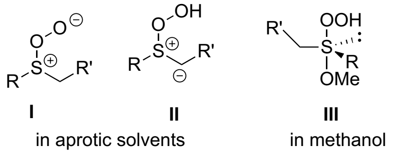
Abstract—Aryl selenides and selenoxides trap efficiently the intermediates in the reaction of singlet oxygen with sulfides. In the co-photooxygenation of 1 equiv of an aryl selenoxide with 1.3 equiv of dimethyl sulfide, the aryl selenone is formed quantitatively. Aryl selenides require 4–5 equiv of sulfide for their complete co-oxidation to selenones.

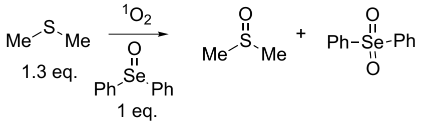
Selenium is an essential trace element for living organisms.[1] It is found mainly in Se-methionine and Se-cysteine, residues of glutathione peroxidase, which functions as an antioxidant catalyzing the reduction of harmful peroxides protecting, therefore, cells from oxidative damage.[2] Due to the antioxidant properties of seleno-compounds their chemistry has recently attracted considerable attention.

In this paper we wish to report our studies on the efficiency of aryl selenides and selenoxides as trapping reagents for the reactive intermediates formed in the reactions of singlet oxygen ($^1O_2$) with sulfides. Reaction of $^1O_2$ with sulfides has been extensively studied in the past and is proposed to proceed, in aprotic solvents, through the formation of two intermediates (Scheme 1), the persulfoxide (**I**) and the *S*-hydroperoxysulfonium ylide (**II**).[3] In protic solvents, such as methanol, formation of the sulfurane intermediate **III** has been postulated.[4]

Several reagents have been reported to trap these reactive intermediates, such as aryl sulfides and sulfoxides,[5] sulfenate and sulfinate esters,[6] sulfinamides,[7] and phosphites.[8] Triphenyl phosphite has been shown to be the most efficient and sulfinamides the worst trapping agent. For example, the relative trapping efficiency of $(PhO)_3P$ against Ph_2SO for the photooxygenation of diethyl sulfide in benzene is ~20.[7] We sought to explore the trapping efficiency of the selenium-analogues of sulfides and sulfoxides. Aryl selenoxides are completely inert against $^1O_2$. However, in the dye-sensitized co-photooxygenation of 1 equiv of diphenyl selenoxide with 1.3 equiv of dimethyl sulfide (dichloromethane, methylene blue as sensitizer), quantitative formation of diphenyl selenone[9] was observed within 3–5 min (Scheme 2). By competing diphenyl selenoxide with diphenyl sulfoxide (a well-known trapping reagent),[5] it was found that selenoxide is 34 ± 4 times more reactive than sulfoxide. Based on this result, diphenyl selenoxide seems to be the most efficient trapping reagent reported so far.[10] Attempts to compare directly the relative trapping efficiency of diphenyl selenoxide with triphenyl phosphite were



Scheme 1. Intermediates in the photooxygenation of sulfides.



Scheme 2. Photooxygenation of dimethyl sulfide in the presence of diphenyl selenoxide.

Keywords: Singlet oxygen; Selenium and compounds; Sulfides; Oxidation.

* Corresponding author. Tel.: +30-2810-393687; fax: +30-2810-393601; e-mail: stratakis@chemistry.uoc.gr

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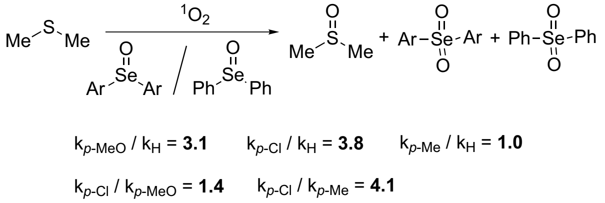
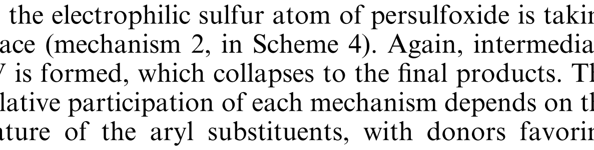


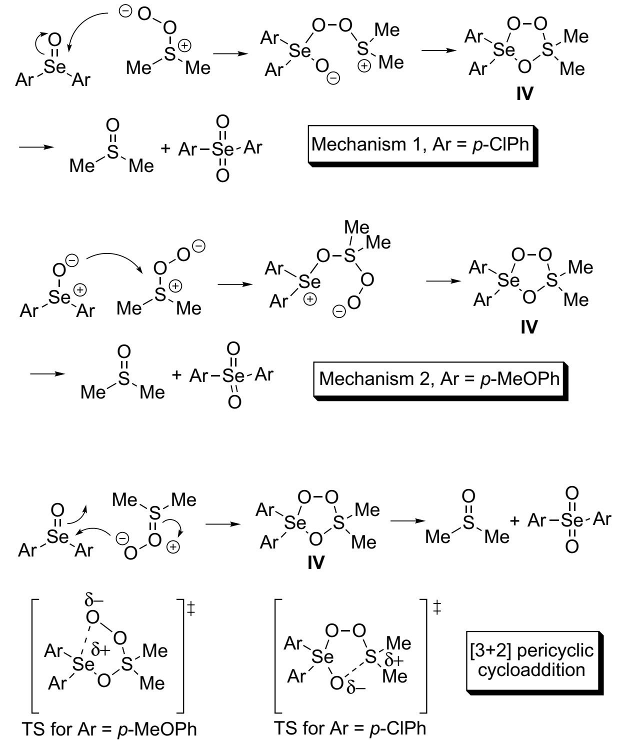
Scheme 3. Competition of aryl selenoxides in their co-photooxygenation with $(CH_3)_2S$.

unsuccessful. Upon mixing diphenyl selenoxide with $(PhO)_3P$, oxygen atom transfer occurs from the selenoxide to phosphite to form a selenide and phosphate.[11]

In a mechanistic study of the selenoxide trapping reaction, we performed kinetic competition for oxidation between diphenyl selenoxide and several aryl selenoxides[12,13] with the sulfide being the limiting reagent. The results are presented in Scheme 3. While *bis*(*p*-methoxyphenyl) selenoxide (electron-donating substituent) is 3.1 times more reactive compared to diphenyl selenoxide, the *bis*(*p*-chlorophenyl) selenoxide (electron-withdrawing substituent) is also 3.8 times more reactive than Ph_2SeO. These results were verified by performing kinetic competition experiments between *p*-Cl- and *p*-MeO-phenyl selenoxides; a relative rate of $k_{Cl}/k_{MeO} = 1.4$, was determined.

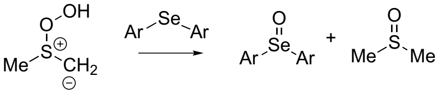
The surprising feature of these results is that both, electron donors (MeO) and electron acceptors (Cl) accelerate the trapping reaction. This can be explained by invoking the two possible mechanisms (1 and 2) shown in Scheme 4. Due to the electron withdrawing substituent (Cl), the Se atom in *bis*(*p*-chlorophenyl) selenoxide is more electrophilic than that of diphenyl selenoxide. Therefore, nucleophilic attack from the negatively charged oxygen of dimethyl persulfoxide to the Se atom can be reasonably assumed to occur, forming the five-membered ring intermediate **IV** (mechanism 1), which in turn, collapses to the products. On the other hand, in *bis*(*p*-methoxyphenyl) selenoxide, the Se atom is significantly less electrophilic compared to diphenyl selenoxide, while the oxygen atom of the Se=O moiety is highly nucleophilic (see resonance structures below). Thus, it is reasonable to assume that nucleophilic attack from the oxygen atom of selenoxide to the electrophilic sulfur atom of persulfoxide is taking place (mechanism 2, in Scheme 4). Again, intermediate **IV** is formed, which collapses to the final products. The relative participation of each mechanism depends on the nature of the aryl substituents, with donors favoring mechanism 2 and acceptors favoring mechanism 1. An alternative rationalization can be envisioned, considering a concerted [3+2] pericyclic cycloaddition to form intermediate **IV**, as shown in Scheme 4. The degree of bond formation in the transition state for the formation of **IV** depends on the nature of the aryl substituents. In the trapping reaction of *bis*(*p*-methoxyphenyl) selenoxide, the new S–O bond has been substantially formed, while the new Se–O bond is very loose and partially formed. On the other hand, in the reaction of *bis*(*p*-chlorophenyl) selenoxide, the Se–O bond has been formed extensively, while the newly formed S–O bond is very loose. We cannot differentiate between the two mechanistic scenarios based on the current results.





Scheme 4. Proposed mechanisms for the trapping reaction of persulfoxide by aryl selenoxides.

In the next step, we examined the efficiency of aryl selenides in trapping the intermediate(s) in the co-photooxygenation with dimethyl sulfide. Their sulfur analogues (aryl sulfides) have been reported[5] to be rather poor trapping reagents. Aryl selenides are unreactive with $^1O_2$ in dichloromethane, even after prolonged photooxygenation times (45 min), in accordance with the recent observations by Krief and Lonez.[14] Yet, in the co-photooxygenation of 2 equiv of dimethyl sulfide with 1 equiv of diphenyl selenide, a mixture of diphenyl selenone (major) and diphenyl selenoxide (minor) were formed (~50–60% conversion of Ph_2Se), indicative that selenides also trap the intermediate(s). By using >4 equiv of dimethyl sulfide relative to diphenyl selenide, almost quantitative conversion to diphenyl selenone was observed. This was also found for the case of *bis*(*p*-chlorophenyl) and *bis*(*p*-methoxyphenyl) selenides, which required approximately 4–5 equiv of dimethyl sulfide to achieve complete oxidation to selenones. It is



Scheme 5. Possible electrophilic oxidation of diaryl selenides by *S*-hydroperoxysulfonium ylide.

more likely that selenides trap the intermediate *S*-hydroperoxysulfonium ylide, which electrophilically transfers an oxygen atom to the Se forming the selenoxide (Scheme 5). The selenoxide in turn traps the persulfoxide intermediate to produce the selenone.

Unfortunately, direct mechanistic conclusions on the selenide trapping reaction (formation of selenoxide), by means of Hammett kinetics, cannot be performed. The main reason is that by mixing an aryl selenide with an aryl selenoxide, oxygen atom transfer occurs to form an equilibrating mixture of the two selenoxides. In addition, since the product from the first trapping reaction (selenoxide) is also a trapping reagent for a different species (persulfoxide), the kinetic analysis is highly complicated.

We wish to point out that these trapping reactions can be used as a novel methodology for the indirect oxidation of selenides and selenoxides to selenones. By performing a preparative scale co-photooxygenation of the selenium compounds (around 0.5 g) with 1.5 equiv of dimethyl sulfide for the case of selenoxides, or 4–5 equiv for the case of selenides, the aryl selenones can be obtained (after washing the organic layer with water to remove dye and DMSO) in >90% isolated yield and >97% purity.

In conclusion, we have shown that organic selenium compounds (aryl selenides and selenoxides) are highly effective trapping agents for the intermediates in the photooxygenation of sulfides. Selenoxides trap the intermediate persulfoxide, while selenides most probably trap the *S*-hydroperoxysulfonium ylide. In addition, aryl selenoxides are the most potent trapping agents reported so far in the literature, trapping the persulfoxide intermediate in an almost quantitative manner.

Acknowledgements

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