Selective deoxygenation of aryl selenoxides by triaryl phosphites. Evidence for a concerted transformation

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Dedicated to Professor G. J. Karabatsos on the occasion of his 70th birthday

Abstract—Triaryl phosphites selectively reduce aryl selenoxides to selenides. The Hammett plot of the reactions of *para*-phenyl substituted triaryl phosphites with diphenyl selenoxide gave $\rho = +2.3$, whereas with bis(*p*-methoxyphenyl) selenoxide, $\rho = -2.1$. The results are consistent with a concerted mechanism for the oxygen transfer from Se to P. © 2002 Elsevier Science Ltd. All rights reserved.

During our ongoing studies on the antioxidant activity of organic selenium compounds, we found that aryl selenoxides can be reduced quantitatively to selenides with equimolar amounts of triaryl phosphites (Scheme 1). The reaction takes place at room temperature in $CHCl_3$ and is complete within 10 min to 2 h depending on the substituents on the aryl rings. Trialkyl phosphites, such as triethyl phosphite, cannot accomplish the reduction to selenides even after 48 h at ambient temperature, whereas diphenyl selenone is completely unreactive with phosphites. Furthermore, aryl sulfoxides are not reduced to sulfides by triaryl phosphites after 24 h at 25°C.

Inorganic phosphorus compounds such as P_2I_4,[1] PI_3,[2] P_4S_{10}[3] and $PSBr_3$[4] are known to reduce (via deoxygenation) very efficiently a variety of compounds such as sulfoxides, selenoxides, amine *N*-oxides, oximes and nitro compounds. The use of organic phosphorus compounds in the deoxygenation of selenoxides to selenides is limited. Dimethyl selenoxide was found by Mikolajczyk and Luckzak[5] to oxidize organic P(III) compounds. The authors postulated nucleophilic attack of phosphorus to the selenium to form a three-membered
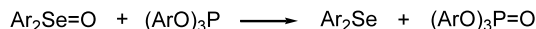
ring intermediate, that collapses to the products. Also, in a specific example, trimethyl phosphite was found[6] to reduce a labile selenoseleninate to a diselenide. Apart from the use of phosphorus compounds, the deoxygenation of selenoxides to selenides can be achieved by several alternative reagents, such as sodium ascorbate,[7] thiourea dioxide,[8] nickel boride,[9] Os(VI) compounds,[10] and a titanocene methylidene complex.[11]

We studied the mechanism for the oxygen transfer from aryl selenoxides to triaryl phosphites by means of kinetics, varying the electronic nature of the substitutents at the *para*-position of phosphorus and selenium compounds. The kinetic competition of triaryl phosphites,[12] for oxidation from the selenoxide, was performed by proton decoupled ^{31}P NMR spectroscopy. The aryl phosphites have resolvable signals in the region of 127–130 ppm,[13] and the product phosphates in the region of −15 to −18 ppm.[13] In a typical example, a mixture of triphenyl phosphite and the *p*-X-substituted triaryl phosphite reacted with diphenyl selenoxide (as limiting reagent in $CDCl_3$) under efficient stirring and after 30 minutes the ^{31}P NMR spectrum was recorded. To ensure accurate integrations of the singlet phosphorus signals, the relaxation delay was maintained at 25 s. The slow competing hydrolysis of triaryl phosphites in $CDCl_3$ was eliminated by adding 1.0 μl of pyridine to the NMR tube.
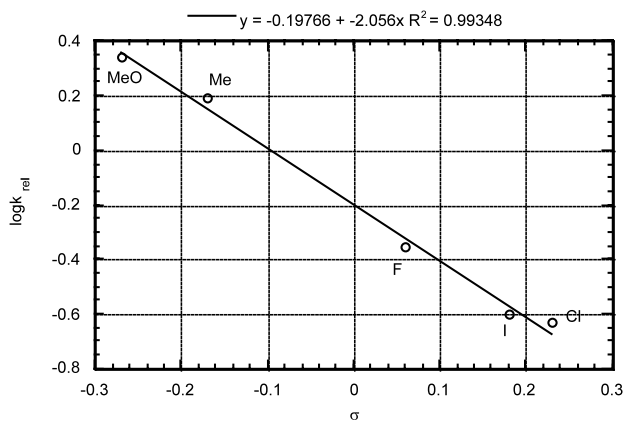
The Hammett plot in the competition of *p*-X substituted triaryl phosphites versus triphenyl phosphite for oxygen atom transfer from diphenyl selenoxide,[14] (Scheme 2) gave a positive slope with $\rho = +2.3$ ($R^2 =$

$$Ar_2Se{=}O \ + \ (ArO)_3P \ \longrightarrow \ Ar_2Se \ + \ (ArO)_3P{=}O$$
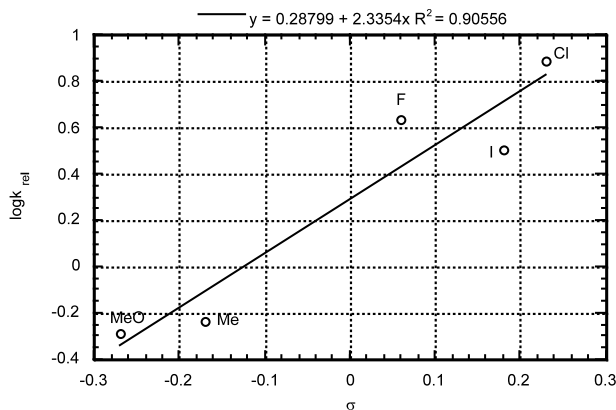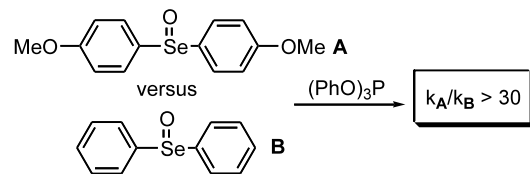
Scheme 1.

Scheme 2. Hammett plot (the values were taken from the textbook *Mechanism and Theory in Organic Chemistry*; Lowry, T. H.; Richardson K. S., 3rd Edition, 1987) in the reaction of triaryl phosphites with diphenyl selenoxide.

0.906). For example, $k_{Cl}/k_H = 7.8 \pm 0.3$, whereas $k_{OMe}/k_H = 0.52 \pm 0.04$. This result indicates that in the transition state of the rate-limiting step, a negative charge has developed on the phosphorus atom. On the other hand, in the competition of the same phosphites with bis(p-methoxyphenyl) selenoxide,[15] completely inverse results were found. For example, $k_{Cl}/k_H = 0.24 \pm 0.02$, whereas $k_{OMe}/k_H = 2.19 \pm 0.06$. The Hammett plot (Scheme 3) gave a negative slope with $\rho = -2.1$ ($R^2 = 0.993$). This result for this specific reaction indicates that a positive charge has developed on the phosphorus atom in the transition state of the reaction.

Apart from the Hammett kinetics presented in Schemes 2 and 3, we performed a kinetic competition of bis-(p-methoxyphenyl) selenoxide with diphenyl selenoxide, for oxygen transfer to triphenyl phosphite. The competition was accomplished by independently reacting the two selenoxides with triphenyl phosphite, and found that bis(p-methoxyphenyl) selenoxide reacts more than 30 times faster than diphenyl selenoxide (Scheme 4). If the kinetic competition is performed by reacting an equimolar mixture of the two selenoxides with triphenyl
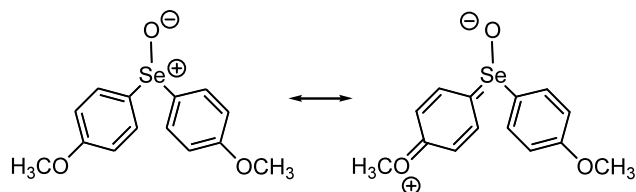

Scheme 4. Competition of bis(p-methoxyphenyl) selenoxide (**A**) with diphenyl selenoxide (**B**) for oxygen atom transfer to triphenyl phosphite.
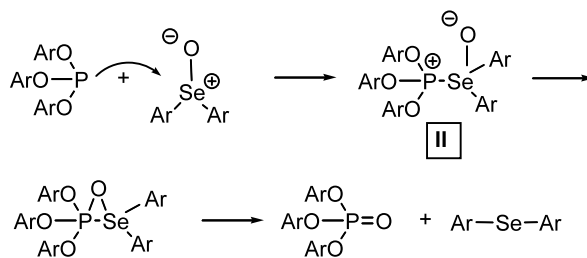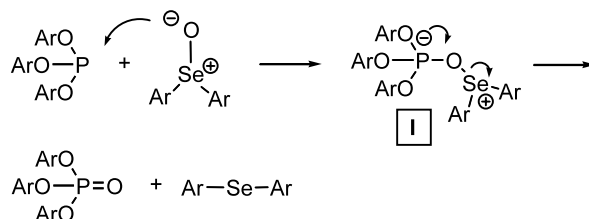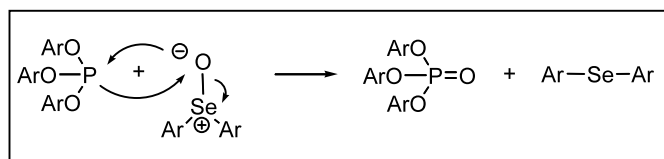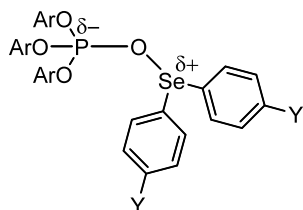

Scheme 5.

phosphite as limiting reagent, equilibration (oxygen transfer) between the selenoxides and the corresponding selenides complicates the kinetic analysis.

By examining the Hammett plots (Schemes 2 and 3) and the results of Scheme 4, it seems that in the reaction with diphenyl selenoxide, triaryl phosphites act as electrophiles,[16] and the oxygen atom of the selenoxide acts as a nucleophile. The possible intermediate **I** (Scheme 5) collapses to the products in a second fast step. With bis(p-methoxyphenyl) selenoxide, one could argue that phosphites act as nucleophiles and attack the selenium atom forming the intermediate **II** (Scheme 5) in the rate-determining step. Formation of the intermediate **II** in the deoxygenation of bis(p-methoxyphenyl) selenoxide, however, is unlikely to occur. The selenium atom in bis(p-methoxyphenyl) selenoxide is less electrophilic compared to diphenyl selenoxide, as seen in the resonance structures below. In addition, the oxygen atom in bis(p-methoxyphenyl) selenoxide is expected to be more nucleophilic.
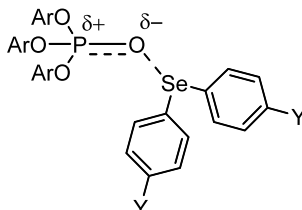

Scheme 3. Hammett plot in the reaction of triaryl phosphites with bis(p-methoxyphenyl) selenoxide.

Transition state for Y = H   **Transition state for Y = OMe**

Scheme 6. Proposed concerted mechanism for the oxygen atom transfer from selenoxides to phosphites.

Thus, attack from the oxygen atom of bis(*p*-methoxyphenyl) selenoxide to the phosphite (intermediate **I**), in agreement with the data of Scheme 4, would be anticipated.

As a reasonable mechanistic rationalization for the observed dramatic changes in the Hammett kinetics, we considered the concerted mechanism shown in Scheme 6. In the transition state for the deoxygenation reaction of diphenyl selenoxide, the O–Se bond is partlialy broken, whereas the oxygen has formed a full σ bond and a partial π bond with phosphorus. Therefore, the P atom bears a partial negative charge ($\delta-$), and the Se a partial positive charge ($\delta+$). In the case of bis(*p*-methoxyphenyl) selenoxide, we propose that the transition state is more 'late' in nature. The positive charge on the Se atom makes the diaryl selenium moiety a better leaving group. Therefore, in the transition state, the Se–O bond is almost completely broken, the π bond has developed significantly between P and O, and the phosphorous atom bears a partial positive charge ($\delta+$). These 'early' and 'late' transition state arguments for a concerted mechanism are in agreement with the Hammett kinetics, and the fact that bis(*p*-methoxyphenyl) selenoxide is more reactive compared to diphenyl selenoxide. A mechanism involving nucleophilic attack of P to Se, as proposed earlier,[5] is rigorously ruled out.

To the best of our knowledge, this work represents the first example in the literature where the sign of the ρ value in a Hammett plot is reversed without a significant change in the reaction mechanism (for both selenoxides, the reaction arises from nucleophilic attack of the oxygen atom to the phosphorus). Further work to examine the mechanistic details of similar oxygen atom transfer reactions are currently in progress.

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12. Triaryl phosphites were prepared by reaction of 4 equiv. of the phenols with 1 equiv. of PBr$_3$ in anhydrous diethyl ether (room temperature, 2 h) containing 5 equiv. of pyridine.
13. The ^{31}P NMR data (in ppm) of the triaryl phosphites (*p*-X-C$_6$H$_4$O)$_3$P and the corresponding phosphates (*p*-X-C$_6$H$_4$O)$_3$P=O are as follows. Phosphites: X=H, 128.63; X=F, 128.20; X=Me, 129.18; X=I, 127.16; X=Cl, 127.55; X=OMe, 129.55. Phosphates: X=H, −17.03; X=F, −16.31; X=Me, −16.33; X=I, −17.66; X=Cl, −17.18; X=OMe, −15.33.
14. Diphenyl selenoxide was prepared by oxidation of diphenyl selenide with *N*-chlorosuccinimide followed by alkaline hydrolysis as described in the literature: Detty, M. R. *J. Org. Chem.* **1980**, *45*, 274–279.
15. Bis(*p*-methoxyphenyl) selenoxide is commercially available from TCI (Japan).
16. For a previous example of nucleophilic oxygen atom transfer to phosphites, see: Stratakis, M.; Orfanopoulos, M.; Foote, C. S. *Tetrahedron Lett.* **1991**, *32*, 863–866.