Reaction of Stable Sulfenic and Selenenic Acids Containing a Bowl-type Steric Protection Group with a Phosphine. Elucidation of the Mechanism of Reduction of Sulfenic and Selenenic Acids

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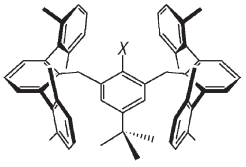
The mechanism of the reduction of the stable sulfenic acid **1** and selenenic acid **2** containing a bowl-type steric protection group by triphenylphosphine was elucidated by tracer studies using $H_2{}^{18}O$. It was found that the initial step of the reaction involves the attack of the phosphine on the sulfur or selenium atom of **1** and **2**, respectively, in contrast with the reduction of hydroperoxides by a phosphine, where the initial attack occurs on the hydroxylic oxygen.

Sulfenic acids (RSOH) and selenenic acids (RSeOH) are well recognized as important intermediates in organic and biochemical reactions of sulfur and selenium compounds.[1,2] They can be regarded as sulfur and selenium analogs of hydroperoxides (ROOH) and their properties as oxidizing agents have been attracting wider attention in view of their critical role in redox regulation in some enzymatic reactions.[3,4] Under non-enzymatic conditions, however, little information has been obtained about oxidation reactions by sulfenic acids or selenenic acids because of their notorious instability; they readily undergo self-condensation to the corresponding thiosulfinates[1] or selenoselenates,[2,5] respectively. While the mechanism of the reduction of hydroperoxides by trivalent phosphorus compounds has been elucidated in detail,[6] no such mechanistic study has been performed on the reaction of sulfenic and selenenic acids. We previously reported the synthesis of the stable sulfenic acid **1**[7] and selenenic acid **2**[8] containing a novel bowl-type steric protection group (denoted as Bmt).[9] In this communication, we present the mechanistic elucidation of the reduction of sulfenic and selenenic acids by a phosphine by taking advantage of these stable sulfenic and selenenic acids.



≡ Bmt*X*

1 (*X* = SOH)
2 (*X* = SeOH)

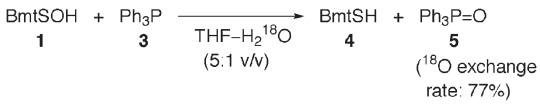
It has been suggested that trivalent phosphorus reagents reduce transiently-generated sulfenic acids.[10] We previously reported that the reaction of BmtSOH (**1**) with triphenylphosphine (**3**) produced BmtSH (**4**) and triphenylphosphine oxide (**5**) almost quantitatively.[7] There has been no report in the literature on the reaction of a selenenic acid with trivalent phosphorus reagents. Treatment of selenenic acid **2** with an equimolar amount of phosphine **3** in THF at room temperature resulted in the quantitative formation of selenol **6** and phosphine oxide **5**, which was confirmed by the ^1H and ^{31}P NMR spectra of the reaction mixture (Scheme 1). These results demonstrate that sulfenic acids and selenenic acids have an oxidizing ability similar to that of hydroperoxides.

Scheme 1.

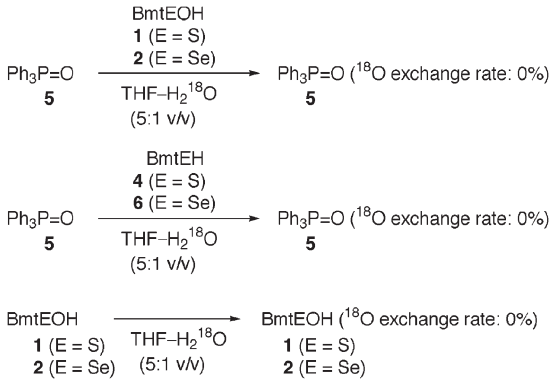
Two possible mechanisms were considered for the reduction of hydroperoxides with trivalent phosphorus reagents.[6b] One mechanism involves the initial attack of the phosphorus on the hydroxylic oxygen atom to form the intermediate **I**, and the other involves the alkoxyphosphonium hydroxide intermediate **II**. In 1960, Denny et al. provided evidence ruling out the alkoxyphosphonium intermediate **II** and supporting the involvement of intermediate **I** by a tracer study using $H_2{}^{18}O$.[6b] They showed that cumyl hydroperoxide was reduced with phosphine **3** in ethanol–$H_2{}^{18}O$ to give cumyl alcohol and phosphine oxide **5**, neither of which contained oxygen-18. This is inconsistent with the formation of intermediate **II**, which should be accompanied by equilibrium between the hydroxide ion and $H_2{}^{18}O$.

Since it has been found that sulfenic acid **1** and selenenic acid **2** oxidize phosphine **3** to phosphine oxide **5** as do hydroperoxides, it is intriguing whether the reaction mechanism is the same as that of hydroperoxides or not. Tracer experiments similar to those of Denny et al. were carried out with **1** and **2**. Sulfenic acid **1** was allowed to react with phosphine **3** in a mixture of THF–$H_2{}^{18}O$ (^{18}O content: 19.2%), and the electron impact mass spectrometry analysis of the resulting phosphine oxide **5** indicated that it contains oxygen-18 in 14.7 atom%, which corresponds to the exchange rate of 77% (Scheme 2). Under the same conditions, the reaction of *t*-butyl hydroperoxide with phosphine **3** gave phosphine oxide **5** containing no oxygen-18, which is in agreement with the results of Denny et al. By control experiments, it was confirmed that no exchange of oxygen between phosphine oxide **5** and $H_2{}^{18}O$ occurs in the presence of either sulfenic acid **1** or thiol **4** (Scheme 3). The absence of exchange of oxygen between **1** and $H_2{}^{18}O$ was also confirmed (Scheme 3).

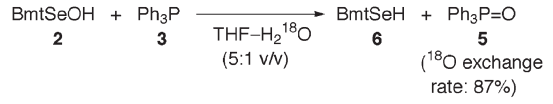
Similar results were obtained in the reduction of selenenic acid **2**. The reaction of selenenic acid **2** with phosphine **3** in THF–$H_2{}^{18}O$ (^{18}O content: 19.2%) produced phosphine oxide **5** containing oxygen-18 in 16.7 atom%, which corresponds to the exchange rate of 87% (Scheme 4). In the control experiments,



Scheme 2.



Scheme 3.

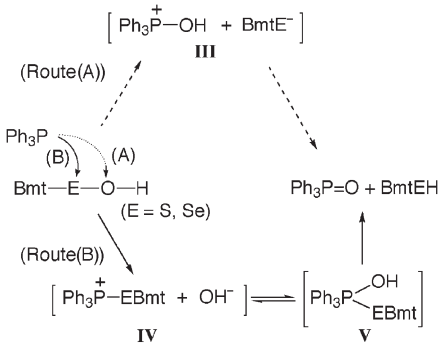


Scheme 4.

no exchange of oxygen atom either between phosphine oxide **5** and $H_2{}^{18}O$, or between **2** and $H_2{}^{18}O$ was observed (Scheme 3).

The incorporation of oxygen-18 in **5** at the high exchange rates of 77 and 87% indicates that the reactions proceed via the initial attack of the phosphorus atom of **3** on the sulfur atom of **1** or the selenium atom of **2** to give the intermediate IV (Route (B) in Scheme 5), not on the hydroxylic oxygen to give the intermediate III (Route (A)). Although the possibility that very small portions of these reactions proceed via Route (A) cannot be ruled out, undoubtedly Route (B) is predominant in contrast with the reduction of hydroperoxides. The arylthio- or arylselenophosphonium intermediate IV is considered to yield the products via the pentacoordinated species V. It may be noted that the nucleophilic attack of a relatively bulky phosphine **3** occurs at the sulfur and selenium atoms, even though they are incorporated in the cavity of the Bmt group and less accessible than the hydroxylic oxygen on steric grounds. It is likely that such high electrophilic character of the sulfur and selenium atoms of sulfenic and selenenic acids plays an important role in their function as oxidizing agents in biological systems.

In summary, the mechanism of the reduction of sulfenic and selenenic acids by a phosphine was elucidated for the first time by taking advantage of stable compounds containing a bowl-type steric protection group. Further investigations on the mechanism of their reactions with other substrates are currently in progress.



Scheme 5.

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References and Notes

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