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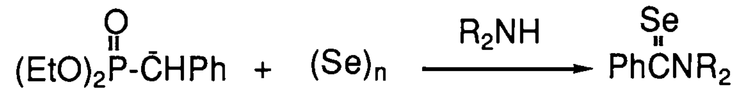
Reactions of Phosphonate Carbanions with Selenium or Sulfur in the Presence of Amines. Synthesis of Seleno- and Thioamides

Kentaro OKUMA,* Koumei IKARI, and Hiroshi OHTA
Department of Chemistry, Faculty of Science, Fukuoka University, Jonan-ku, Fukuoka 814-01

The reaction of phosphonate carbanions with elemental selenium in the presence of amines afforded the corresponding selenoamides in moderate yields. The reaction of these anions with sulfur also gave thioamides. These reactions might proceed through thio- or selenoaldehyde intermediates.

The chemistry of selenoamides (**1**) is of current interest.$^{1)}$ Recently, we have reported the reaction of phosphonium ylides with sulfur followed by the addition of amines afforded the corresponding thioamides (**2**) in good yields.$^{2)}$ However, selenoamides (**1**) could not be obtained by this method. Mikołajczyk *et al.* reported the reaction of phosphonate carbanions (**3**) with elemental sulfur or selenium to afford the corresponding thiols or selenols.$^{3)}$ They used these thiols or selenols for the synthesis of natural products.$^{4)}$ These results prompted us to investigate the reaction of **3** with selenium and amines. In this communication, we report a new synthesis of **1** and **2** by the reaction of **3** with selenium (or sulfur) and amines.

We first tried the reaction of **3** with selenium in the presence of amines. To a solution of benzyldiethylphosphonate in THF was added sodium hydride and stirred for 1 h. Elemental selenium and morpholine were added to this solution and refluxed for 5 h. After the usual work-up of the reaction mixture, chromatographic separation of the residue on silica gel afforded 12% yield of selenobenzmorpholide (**1a**) as yellow crystals. Other reactions were carried out in a similar manner (Table 1). Lower yields of the selenoamides in this reaction might be owing to the low solubility of selenium.



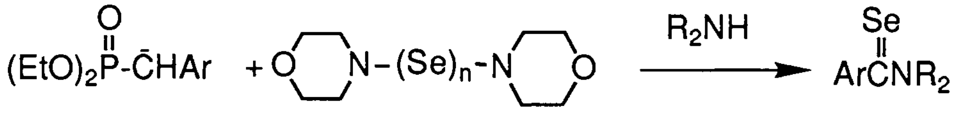
$$(\mathrm{EtO})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}\text{-}\bar{\mathrm{C}}\mathrm{HPh} + (\mathrm{Se})_n \xrightarrow{\mathrm{R_2NH}} \mathrm{Ph}\overset{\mathrm{Se}}{\overset{\|}{\mathrm{C}}}\mathrm{NR_2}$$

3a **1**

Table 1. Preparation of Selenoamides (**1**)

Product	Amine	Conditions			Yield/%
		Solvent	Temperature	Time/h	
1a	Morpholine	THF	reflux	37	12
1b	Piperidine	benzene	reflux	20	13
1c	Pyrrolidine	benzene	reflux	20	11

Foss and Janickis prepared aminoselanes (**4**) by the reaction of elemental selenium with amines and Pb_3O_4, which are soluble in many organic solvents.5) The yields of selenoamides were improved by the use of dimorpholinoselanes instead of elemental selenium (Table 2). On the other hand, the reaction of phosphonium ylides with elemental selenium afforded the corresponding bis(dialkylamino)-alkanes.2) The difference in reactivity might be due to the difference in nucleophilicity between ylides and phosphonate carbanions. Selenoamides have been formerly prepared by adding hydrogen selenide to a nitrile or by the reaction of mono- or disubstituted amides with phosphorus pentaselenide.6)



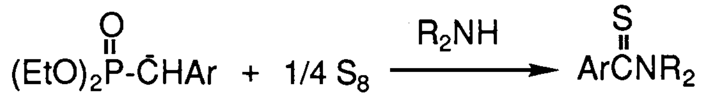
3 (n=2,3, and 4) **4** **1**

Table 2. Preparation of Selenoamides by use of Aminoselane (**4**)

Product	Ar	Amine	Conditions		Yield/%a)
			Solvent	Time/h	
1a	Ph	Morpholine	THF	3	60
1b	Ph	Piperidine	THF	5	44
1c	Ph	Pyrrolidine	THF	5	37
1d	Ph	diethylamine	THF	6	17b)
1e	$4\text{-}CH_3C_6H_4$	Morpholine	THF	7	62

a) Less than 5% of stilbenes were obtained.
b) Selenoamide (**1a**)was also obtained in 35% yield.

Since thioamides (**2**) were already prepared by the reaction of phosphoprus ylides with sulfur, we also applied this method to the reaction of the phosphonate carbanions with elemental sulfur. The corresponding thioamides (**2**) were succesfully prepared. The phosphonate carbanion containing nitro group gave the corresponding thioamide (**2e**) in low yield. We also tried the reaction of triethylphosphonoacetate with butyllithium followed by the addition of sulfur and morpholine. However, the corresponding thiooxamide could not be isolated. Thus, electron-donating groups might be necessary for the preparation of thioamides. The most famous method for the preparation of thioamides is the Willgerodt-Kindler reaction.7) Recently, Fischer *et al.* reported that the reaction of metal-coordinated thioaldehydes with ynamines afforded thioamides.8) However, there is no report on the synthesis of **2** from phosphonate carbanions.



3 **2**

As to the formation of the thioamides, the following mechanism is reasonable. The phosphonate carbanions reacted with sulfur to afford the thioaldehyde intermediates, which converted to the corresponding thioamides in a manner similar to the reaction of phosphonium ylides with sulfur and amines.2) To investigate

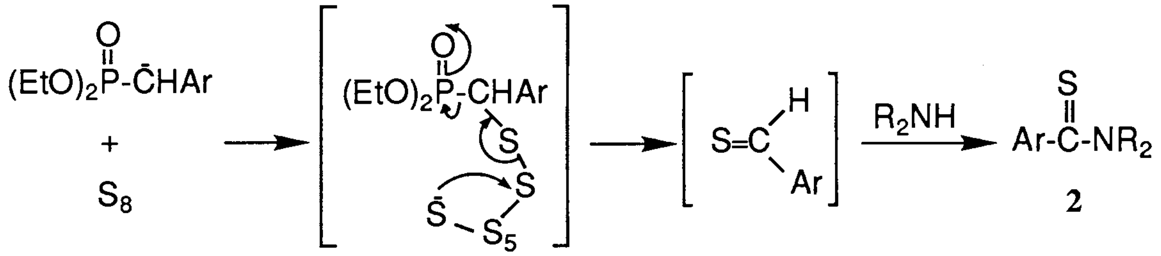
Table 3. Preparation of Thioamides (**2**)

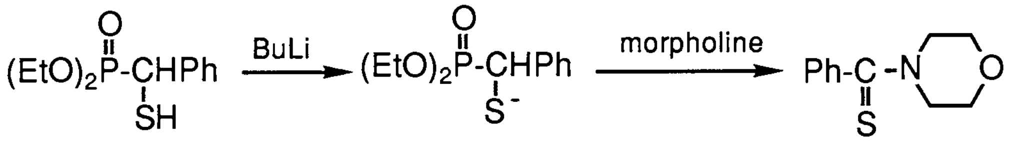
Product	Ar	Amine	Conditions		Yield/%[a]
			Temperature	Time/h	
2a	Ph	Morpholine	reflux	3	60
2a	Ph	Morpholine	40 °C	3	39
2b	Ph	Piperidine	reflux	4	46
2c	Ph	Pyrrolidine	reflux	4	49
2d	4-$CH_3C_6H_4$	Morpholine	reflux	5	65
2e	4-$NO_2C_6H_4$	Morpholine	reflux	7	18

a) Stilbenes were obtained in less than 5% yields.

the mechanism, we tried the reaction of diethyl α-mercaptophenylmethanephosphonate (**5**) with butyllithium followed by the addition of morpholine. The corresponding benzothiomorpholide was obtained in 46% yield along with stilbene (less than 10% yield).

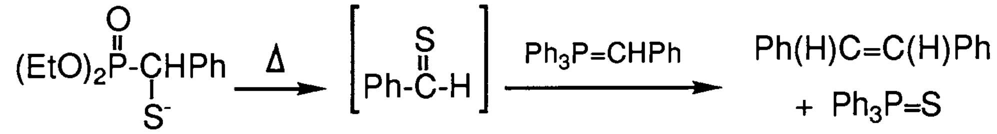
Mechanism





5 **2a**

This result suggested that the reaction proceeded via thioaldehyde intermediates. However, the corresponding Diels-Alder adducts could not be obtained by the reaction of the carbanions with sulfur in the presence of dienes. We then tried the reaction of (phenylmethylene)triphenylphosphorane with diethyl mercaptophenylphosphonate in the presence of butyllithium. *cis-* and *trans-*Stilbenes were obtained in 45% yields. This is another confirmation of thioaldehyde intermediate in this reaction.



The reaction of phosphorus ylides with sulfur was originally carried out by Staudinger and Meyer, which resulted in the formation of thiocarbonyl compounds.9) However, there is no report on the synthesis of thio- or selenocarbonyl compounds from the reaction of phosphonate carbanions with sulfur or selenium.10) The present results will provide the new reaction of phosphonate carbanions with chalcogen compounds such as Horner-Emmons reaction. Efforts to explore the chemistry of thio- and selenoamides and to expand the scope of thio- and selenocarbonyl reactivity are continuing in our labolatories.

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