Zinc-Mediated Cleavage of Diselenides: A Novel Synthesis of Unsymmetrical Diorganyl Selenides in Aqueous Media

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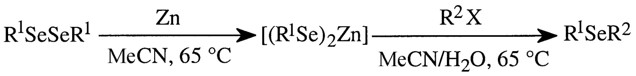
Abstract: A convenient synthetic method has been developed for the preparation of unsymmetrical selenides through a one-pot zinc-mediated reaction of diselenides and active organic halides in aqueous media.

Key words: diselenides, selenides, zinc, zinc selenolate, halides

Organoselenium compounds are of considerable interest because of their wide involvement as key intermediates in organic synthesis and use as a food supplement.[1] These compounds are no longer systematically classified as toxic and, thus, much effort is being devoted to accomplishing the synthesis of organic selenides. Although numerous reports on the synthesis of organoselenium compounds have already been published,[1,2] most of them, with the exception of two recent reports,[3] usually require the handling of unstable reagents, strongly acidic or basic reaction conditions, and two-step procedures. Hence, the development of a one-step synthetic method using stable reagents under neutral conditions is in demand.

In the last decade, organometallic reactions in aqueous media have attracted considerable attention in organic synthesis.[4] Recently, transition metal selenolates or complexes have been widely used in synthesis of organoselenium compounds,[5–7] but reports exploring zinc selenolates are rare.[8–10]

As a part of our work in aqueous organometallic reactions, we wish to report herein that zinc powder promotes cleavage of the Se-Se bond to form selenide anion (RSe^-). This species can then react with active organic halides such as benzyl halides, α-haloesters, α-haloacids, and chloroacetonitrile to afford unsymmetrical selenides in good to excellent yields at 65 °C (Scheme 1). To our knowledge Reformatsky-type reactions in aqueous organometallic reaction conditions are not generally successful.[4b]



$$\underset{\mathbf{1}}{R^1SeSeR^1} \xrightarrow[\text{MeCN, 65 °C}]{\text{Zn}} \underset{\mathbf{2}}{[(R^1Se)_2Zn]} \xrightarrow[\text{MeCN/H}_2\text{O, 65 °C}]{R^2X} \underset{\mathbf{3}}{R^1SeR^2}$$

1 2 3

Scheme 1

We found that under mild, atmospheric, and neutral conditions, zinc benzyl and arylselenolates **2**, readily prepared in situ from the reductive cleavage of the Se-Se bond of dibenzyl and diaryl diselenides, reacted readily with the above halides in acetonitrile–water to give unsymmetrical selenides **3**. All of the reactions studied proceeded smoothly to give the corresponding selenides with yields ranging from 64–98% (Table 1).[11] The reaction of diaryl diselenides with benzyl bromide (entries 1 and 3) took place faster with higher yields than the others. The results clearly show the need for longer reaction times for benzyl chloride (entries 9 and 10), giving the products with lower yields. The effects of several solvents were examined and the best results were obtained with an acetonitrile–water (7:1) system. It is noteworthy that, while diaryl diselenides reacted conveniently with the halides merely in the presence of metallic zinc, the reaction of dibenzyl diselenide (entries 2 and 5) with these halides did not take place in the absence of aluminum chloride. An important feature of this method was seen with bromoacetic acid, which reacted directly with the zinc phenylselenolate intermediate to give α-phenylselenoacetic acid in 73% yield. No evidence was found for the formation of benzeneselenol.

To conclude, an efficient one-pot synthetic method of unsymmetrical selenides has been developed through the zinc-mediated reaction of diselenides with active organic halides. The present method has the advantages of operational simplicity, neutral, mild reaction conditions, high isolated yields of products, lack of toxicity, and low costs.

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Table 1 Preparation of Unsymmetrical Selenides via Zinc Selenolate Anion Intermediate

Entry	R^1	R^2X	Reaction time (h)	Product[a]	Yield (%)[b]
1	Ph	$PhCH_2Br$	0.2	$PhSeCH_2Ph$[12]	98
2[c]	$PhCH_2$	$PhCH_2Br$	5	$PhCH_2SeCH_2Ph$[12]	72
3	p-ClC_6H_4	$PhCH_2Br$	0.5	p-$ClC_6H_4SeCH_2Ph$[13]	98
4	Ph	$BrCH_2CO_2Et$	1	$PhSeCH_2CO_2Et$[14]	89
5[c]	$PhCH_2$	$BrCH_2CO_2Et$	5.5	$PhCH_2SeCH_2CO_2Et$[15]	70
6	p-ClC_6H_4	$BrCH_2CO_2Et$	3	p-$ClC_6H_4SeCH_2CO_2Et$[15]	71
7	Ph	$ClCH_2CN$	4	$PhSeCH_2CN$[14]	82
8	p-ClC_6H_4	$ClCH_2CN$	6	p-$ClC_6H_4SeCH_2CN$[15]	87
9	Ph	$PhCH_2Cl$	3	$PhSeCH_2Ph$[12]	64
10	p-ClC_6H_4	$PhCH_2Cl$	2	p-$ClC_6H_4SeCH_2Ph$[12]	66
11	Ph	$CH_3CHBrCO_2CH_3$	5.5	$PhSeCH(CH_3)CO_2CH_3$[16]	77
12	Ph	$BrCH_2CO_2H$	6	$PhSeCH_2CO_2H$[14]	73

[a] References of the known compounds.

[b] Yields refer to those of pure isolated products characterized by IR and ^1H NMR spectroscopic data.

[c] In the presence of $AlCl_3$.

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(11) **General Experimental Procedure.** In a 50 mL round-bottom flask, fitted with a reflux condenser, were placed zinc powder (0.5 mmol), diorganyl diselenide (4 mmol), and MeCN (14 mL). (In the case of dibenzyl diselenide, $AlCl_3$ (1.5 mmol) was also added at this stage.) The mixture was stirred at 65 °C for 1 h until the zinc powder was almost consumed and the solution became turbid; organic halide (1.8 mmol) and H_2O (2 mL) were then added at once to the solution and stirring was continued for the specified time (Table 1) at 65 °C. Progress of the reaction was monitored by TLC. When the reaction was complete, MeCN was evaporated, Et_2O (30 mL) was added, the mixture washed with H_2O (3 × 20 mL), and the organic layer was dried over anhyd Na_2SO_4. The solvent was evaporated in vacuo to give the corresponding selenide which was purified by preparative TLC (silica gel, eluent petroleum ether–CCl_4 = 1:1 or petroleum ether–Et_2O = 9:1 or CCl_4–Et_2O = 4:1).

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