Reductive Cleavage of the Se–Se Bond by the Sm–Me$_3$SiCl–H$_2$O System: Preparation of Unsymmetrical Phenyl Selenides†

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The reduction of diphenyl diselenide by the Sm–Me$_3$SiCl–H$_2$O system led to a selenide anion. This 'living' species reacted with organic halides, epoxides, α,β-unsaturated esters and α,β-unsaturated nitriles to afford unsymmetrical phenylselenides in good yields under mild and neutral conditions.

Organoselenium compounds have received considerable attention as useful synthetic reagents and intermediates in organic synthesis.[1] While there are many methods for the introduction of a seleno-substituent into organic molecules, the use of phenyl selenide anions is especially convenient and common. Several methods for the synthesis of selenide anions have been recommended, the more important of which include the use of diphenyl diselenide with sodium borohydride,[2] reduction of the diselenide with sodium,[3] samarium diiodide[4] and lithium aluminium hydride.[5] Alternatively, sodium phenyl selenide may be obtained from the selenol using sodium hydride or even by treatment with aqueous sodium hydroxide under certain conditions.[6] Moreover, Grignard reagents also react with selenium to give selenide anions.[7]

As a powerful, versatile and either-soluble one-electron transfer reducing agent, SmI$_2$ has been widely applied in organic synthesis.[8] Though SmI$_2$ is a useful reagent, storage is difficult because it is very sensitive to air oxidation. On the other hand, metallic samarium is stable in air and its strong reducing power (Sm^{3+}/Sm −2.41 V) is similar to that of magnesium (Mg^{2+}/Mg −2.37 V) and superior to that of zinc (Zn^{2+}/Zn −0.71 V). These properties prompted us to use the more convenient and cheaper samarium directly as a reductant instead of samarium(II) iodide. Recently, there have been reports on the direct use of Sm in organic synthesis.[9] Ishii and co-workers have shown that the Sm–Me$_3$SiCl–NaI and Sm–Me$_3$SiBr systems can be used for the intermolecular carbon–carbon bond formation reaction of carbonyl compounds.[10] Herein, we report that the Sm–Me$_3$SiCl–H$_2$O system promotes cleavage of the Se–Se
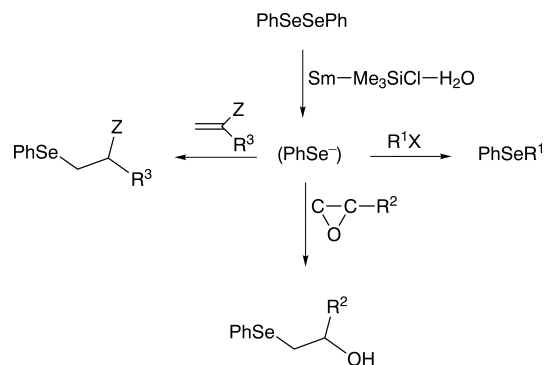
Scheme 1

bond to form a phenyl selenide anion. This species reacted with organic halides, epoxides, α,β-unsaturated esters and α,β-unsaturated nitriles to afford unsymmetrical phenyl-selenides in good yields under mild and neutral conditions. The results are summarized in Table 1.

We found that under mild conditions, phenyl selenide anion, readily prepared *in situ* from the cleavage of the Se–Se bond of diphenyl diselenide with the Sm–Me$_3$SiCl–H$_2$O reduction system, reacted easily with epoxides, α,β-unsaturated esters and α,β-unsaturated nitrile respectively to afford the desired unsymmetrical alkyl phenyl selenides in good yields. From Table 1, we also found that the phenyl selenide anion, a 'living' species, reacted smoothly with active organic halides such as 2-bromoacetophenone and ethyl bromoacetate to give products in good yields at 45 °C.

Table 1 Preparation of unsymmetrical phenyl selenides *via* phenyl selenide anion intermediate

Entry	R^{1}X	R^2	R^3	Z	$T/^\circ$C	t/h	Yield (%)^a
a	PhCH$_2$Cl				65	4	75
b	PhCOCH$_2$Br				45	3	72
c	BrCH$_2$CO$_2$Et				45	3	66
d	n-C$_4$H$_9$Br				65	4	68
d^b	n-C$_4$H$_9$Br				65	4	32
e	n-C$_4$H$_9$Cl				65	10	—
f	n-C$_6$H$_{13}$Br				65	4	70
g	n-C$_8$H$_{17}$Br				65	4	72
h		H			45	2	80
i		CH$_2$Cl			45	2	82
j			H	CN	45	2	79
k			H	CO$_2$Me	45	2	84
l			Me	CO$_2$Me	45	2	83

^{a}Isolated yields. Reaction conditions: diphenyl diselenide (0.5 mmol), Sm (1.0 mmol), Me$_3$SiCl (1.0 ml), THF (5 ml), H$_2$O (18 μl), cleavage reaction temperature, 45 °C, 3 h. ^{b}In the absence of water.

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With the less active halides R^{2}X such as alkyl bromides and benzyl chloride, the coupling reaction should be carried out at a higher temperature (65 °C). Unfortunately, alkyl

chloride gives too little product to be isolated even with a longer reaction time (entry **e**).

The result of our experiment indicated that as a small amount of water was added to the Sm–Me₃SiCl system, it not only accelerated the cleavage reaction, but also increased the yield of product. However, the mode of action is not fully understood and a more detailed study is in progress in our laboratory.

In conclusion, it has been found that the Sm–Me₃SiCl–H₂O reductive system is an effective one for cleaving the Se–Se bond in diphenyl diselenide at mild temperatures. The notable advantages of this reaction are neutral reaction conditions, simple operation and good yields.

Experimental

^{1}H NMR spectra were recorded on a JEOL PMX 60 SI instrument. All NMR samples were measured in CCl_4 using Me_4Si as internal standard. IR spectra were obtained on a Perkin-Elmer 683 spectrophotometer as liquid films.

Metallic samarium and other chemicals were purchased from commercial sources and used without purification. Chlorotrimethylsilane was redistilled prior to use and kept under an inert atmosphere with molecular sieves. THF was freshly distilled from sodium–benzophenone ketyl prior to use.

General Procedure for the Preparation of Unsymmetrical Phenyl Selenides.—Under a nitrogen atmosphere, metallic samarium powder (0.15 g, 1.0 mmol) and diephenyl diselenide (0.16 g, 0.5 mmol) were placed in a three-necked reaction flask and Me₃SiCl (1.0 ml) and THF (5 ml) were added in one portion. Then H_2O (18 μl) was added to the mixture and the resulting mixture was magnetically stirred for 3 h at 45 °C until the powdered samarium was almost consumed and the yellow solution had become almost colorless. To the mixture was added organic halide (1.2 mmol), (or epoxides, *etc.*) in THF (5 ml). When the reaction was complete, water (4 ml) was added to quench the reaction and the mixture was extracted with diethyl ether (2 × 20 ml). The extracts were washed with brine, dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure; the residue was then purified by preparative TLC on silica gel to give pure product.

Benzyl phenyl selenide.[11] Oil. δ_H 3.95 (2 H, s, CH₂Se), 7.05–7.45 (10 H, m, ArH). ν_{max}/cm^{-1} 3090, 2980, 1580, 1490, 1440, 1150, 940, 740, 690.

2-(Phenylseleno)acetophenone.[4] Oil. δ_H 4.05 (2 H, s, CH₂Se), 7.00–7.95 (10 H, m, ArH). ν_{max}/cm^{-1} 3085, 2960, 1682, 1600, 1590, 1480, 1410, 1275, 1180, 925, 735, 700, 680.

Ethyl 2-(phenylseleno)acetate.[12] Oil. δ_H 1.12 (3 H, t, CH₃), 3.29 (2 H, s, CH₂Se), 3.96 (2 H, q, OCH₂), 7.01–7.65 (5 H, m, ArH). ν_{max}/cm^{-1} 3070, 2960, 1750, 1590, 1485, 1460, 1350, 1220, 1170, 935, 740, 690.

Butyl phenyl selenide.[13] Oil. δ_H 0.80 (3 H, t, CH₃), 1.00–1.85 [3 H, m, (CH₂)₂], 2.70 (2 H, t, CH₂Se), 6.95–7.55 (5 H, m, ArH). ν_{max}/cm^{-1} 3050, 2950, 1590, 1470, 1420, 1370, 1220, 1115, 920, 735, 700.

Hexyl phenyl selenide.[14] Oil. δ_H 0.80 (3 H, t, CH₃), 1.00–1.95 [8 H, m, (CH₂)₄], 2.95 (2 H, t, CH₂Se), 7.00–7.60 (5 H, m, ArH). ν_{max}/cm^{-1} 3040, 2940, 1580, 1480, 1420, 1380, 1230, 1100, 930, 740, 690.

Octyl phenyl selenide.[15] Oil. δ_H 0.80 (3 H, t, CH₃), 1.00–2.10 [12 H, m, (CH₂)₆], 3.20 (2 H, t, CH₂Se), 7.02–7.70 (5 H, m, ArH). ν_{max}/cm^{-1} 3020, 2945, 2860, 1589, 1460, 1400, 1220, 1110, 1041, 928, 790, 740, 690.

2-(Phenylseleno)ethanol.[16] Oil. δ_H 2.34 (1 H, s, OH, disappeared on adding D₂O), 2.90 (2 H, t, CH₂Se), 3.59 (2 H, t, CH₂O), 7.00–7.54 (5 H, m, ArH). ν_{max}/cm^{-1} 3530, 3040, 2955, 2900, 1600, 1490, 1462, 925, 740, 700.

1-Chloro-3-(phenylseleno)propan-2-ol.[17] Oil. δ_H 2.73 (1 H, s, OH, disappeared on adding D₂O), 3.00 (2 H, d, CH₂Se), 3.52 (2 H, d, CH₂Cl), 3.64–4.00 (1 H, m, CH), 7.03–7.49 (5 H, m, ArH). ν_{max}/cm^{-1} 3450, 2089, 3050, 2945, 2900, 1590, 1485, 1460, 1050, 1020, 940, 735, 700.

β-(Phenylseleno)propionitrile.[18] Oil. δ_H 2.30–2.70 (2 H, m, CH₂CN), 2.74–3.13 (2 H, m, CH₂Se), 7.00–7.52 (5 H, m, ArH). ν_{max}/cm^{-1} 3100, 3080, 2950, 2254, 1588, 1485, 1445, 1420, 1070, 1020, 932, 735, 685.

Methyl 3-(phenylseleno)propanate.[15] Oil. δ_H 2.33–2.77 (2 H, m, CH₂CO₂R), 2.80–3.18 (2 H, m, CH₂Se), 3.50 (3 H, s, OCH₃), 6.97–7.53 (5 H, m, ArH). ν_{max}/cm^{-1} 3060, 2965, 1750, 1590, 1485, 1460, 1355, 1225, 1165, 1021, 935, 735, 690.

Methyl 2-methyl-3-(phenylseleno)propanate.[19] Oil. δ_H 1.1–1.2 (3 H, d, CH₃), 2.40–2.60 (2 H, m, CH), 2.65–3.20 (2 H, m, CH₂Se), 3.54 (3 H, s, OCH₃), 7.00–7.65 (5 H, m, ArH). ν_{max}/cm^{-1} 3065, 2950, 1745, 1590, 1480, 1450, 1360, 1230, 1170, 930, 730, 690.

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