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Indium-mediated cleavage of diphenyl diselenide and diphenyl disulfide: efficient one-pot synthesis of unsymmetrical diorganyl selenides, sulfides, and selenoesters

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ABSTRACT

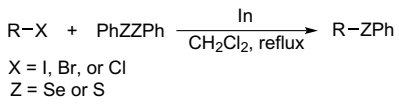
A convenient and efficient method was developed for the synthesis of alkyl phenyl selenides, sulfides, and selenoesters in one-pot reaction by using indium metal. The reaction showed the selectivity for *tert*-alkyl, benzylic, and allylic halides over primary and secondary alkyl halides. For the reaction of primary and secondary alkyl iodides and bromides, the yields of selenides were improved by the addition of a catalytic amount of iodine.

1. Introduction

Interest in organochalcogenides has increased continuously for their important role in organic synthesis and their useful biological activities. Organoselenium compounds, for instance, have been proved to play a role as important therapeutic compounds such as antiviral and anticancer agents.[1] Organochalcogenides have also emerged as crucial intermediates in the transformations of a variety of functional groups.[2]

Much effort has been devoted to accomplish the synthesis of organochalcogenides, and a number of reports on the preparation of organochalcogenides have been published.[3,4] However, many preparative methods proceeded with multi-step procedures under strongly basic or acidic reaction conditions and sometimes suffered from improper handling of unstable reagents in air and moisture. Therefore, development of new synthetic methods is required in organic synthesis for the preparation of organochalcogenides using stable reagents and one-step procedure under neutral conditions.

Over the past decade, indium metal and its salts have been chosen as the reagents for carbon–carbon bond formation, rearrangements, and a variety of useful reactions.[5] They have drawn an increasing attention for their unique properties such as low toxicity and high stability in water and air compared with other metals. As part of our effort toward developing applications of indium metal in organic synthesis,[6] we developed an indium-mediated reaction for preparing unsymmetrical organochalcogenides from alkyl halides and diphenyl diselenide (diphenyl disulfide).[7] Herein, we wish to report an account on a mild and efficient one-pot procedure for the synthesis of alkyl phenyl selenides, sulfides, and selenoesters using indium metal under neutral conditions (Scheme 1).



Scheme 1.

2. Results and discussion

We first performed the reaction of ^{t}BuCl with PhSeSePh under various reaction conditions as shown in Table 1. The reaction of

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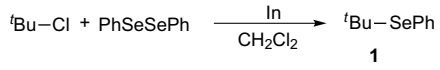
Table 1
Reaction of ^{t}BuCl with PhSeSePh in the presence of indium



Entry	^{t}BuCl (equiv)	In (equiv)	Temp	Time (h)	Yield[a] (%)
1	2.0	1.0	Reflux	1	95
2	2.0	1.0	rt	3	99
3	2.0	0	Reflux	1	0
4	2.0	0.5	Reflux	1	91
5	2.0	0.1	Reflux	1	20
6	2.0	1.0	Reflux	1	3[b]

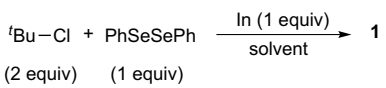
[a] The reaction was analyzed by GC, and the yield was calculated on the base of the amount of ^{t}BuCl.
[b] $InCl_3$ was used instead of In.

diphenyl diselenide with 2.0 equiv of ^{t}BuCl in the presence of an equimolar amount of indium in CH_2Cl_2 at reflux for 1 h afforded *tert*-butyl phenyl selenide (**1**) in 95% yield, which was determined on the base of the amount of ^{t}BuCl (entry 1). When the reaction was carried out at ambient temperature, a quantitative yield of the product was obtained (entry 2), although longer reaction time was required for completion. In the absence of indium metal, however, the reaction did not proceed at all, implying that indium acts as a promoter of the reaction (entry 3). The essential amount of indium required for efficient promoting of the reaction could be reduced to 0.5 equiv affording the product in 91% yield (entry 4). With 0.1 equiv of indium (entry 5) or 1.0 equiv of $InCl_3$, the reaction was not efficient (entry 6).

Next, we investigated the solvent effects on the reaction (Table 2). The reaction of ^{t}BuCl with PhSeSePh in common organic solvents including benzene, toluene, THF, and CH_3CN at ambient temperature and boiling temperature of the solvents gave the product **1** in low to moderate yields. At room temperature, chlorinated solvents such as CH_2Cl_2 (Table 1, entry 2) and $ClCH_2CH_2Cl$ (Table 2, entry 4) were optimal. However, the yield of the product **1** decreased dramatically at the boiling temperature of $ClCH_2CH_2Cl$ (entry 4). We thought that it might be related with the thermal stability of the product **1**. In controlled experiments, it was found that the reaction in CH_2Cl_2 was completed within 3 h at room temperature and in 1 h at reflux giving quantitative yields of the product. On the other hand, when the reaction time increased to 24 h in both cases, it caused a decrease in the yield of the product to 80% and 70%, respectively. Thus, it proved that the prolonged reaction time gave a detrimental effect on the yield of the product. We also carried out the reaction in aqueous CH_2Cl_2 to afford a low yield of the product (entry 6). Notably, CH_2Cl_2 was the solvent of choice.

Under optimal reaction conditions, a variety of sterically diverse organic halides brought into the reaction with diphenyl diselenide in order to evaluate the scope and limitations of the present procedure. The results are presented in Table 3. Tertiary alkyl halides underwent a clean reaction to provide the corresponding alkyl phenyl selenides in high yields (entries 1–5). Note that the reaction of *tert*-alkyl halides with metal phenyl selenolates, which were made from the reaction of PhSeSePh with La[4m] or Zn,[4o] or from the reaction of PhSeH with CsOH,[4h] could not be achieved even under harsh reaction conditions. It is interesting to note that the reaction with bridged halides, 1-haloadamantanes, also proceeded without difficulty (entries 3–5). Various primary and secondary alkyl halides were examined. In contrast to tertiary alkyl halides, they were found to be inactive to the present indium-promoted selenation of alkyl halides (entries 6–9). Benzyl phenyl selenides were also formed from benzyl bromide and chloride (entries 10–15). With substituent groups on benzene

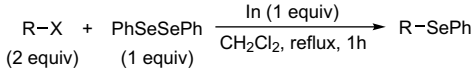
Table 2
Solvent effects on the reaction of ^{t}BuCl with PhSeSePh in the presence of indium

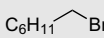
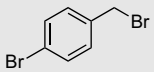
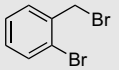
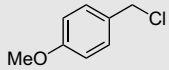
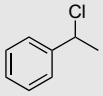
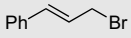
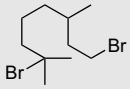


Entry	Solvent	Yield[a,c] (%)	Yield[b,c] (%)
1	Benzene	51	65
2	Toluene	38	41
3	THF	0	22
4	$ClCH_2CH_2Cl$	99	52
5	CH_3CN	50	66
6	CH_2Cl_2/H_2O (9:1, v/v)	—	42

[a] The reaction was carried out at room temperature for 3 h.
[b] The reaction was carried out in a boiling solvent for 1 h.
[c] The reaction was analyzed by GC, and the yield was calculated on the base of the amount of ^{t}BuCl.

Table 3
Synthesis of alkyl phenyl selenides from alkyl halides



Entry	RX	RSePh	Yield[a] (%)
1	^{t}BuI	**1**[b]	99
2	^{t}BuBr	**1**[b]	95 (86)
3	1-Iodoadamantane	**2**[c]	86 (76)
4	1-Bromoadamantane	**2**[c]	84 (74)
5	1-Chloroadamantane	**2**[c]	99 (88)
6	^{i}PrI	**3**[d]	NR
7	Cyclohexyl bromide	**4**[d]	NR
8	$CH_3(CH_2)_5I$	**5**[e]	NR
9		**6**	NR
10	$PhCH_2Br$	**7**[f]	86 (70)
11		**8**[g]	98 (85)
12		**9**	99 (95)
13	$PhCH_2Cl$	**7**[f]	- (84)
14		**10**[d]	- (52)
15		**11**[d]	67 (59)
16		**12**[b]	99 (89)
17		**12**[b]	97 (73)
18		**13**[d]	40 (32)
19	PhBr	**14**[h]	NR
20	PhI	**14**[h]	NR
21		**15**[i]	85

[a] The reaction was analyzed by GC, and the yield was calculated on the base of the amount of RX. The yields in parentheses are isolated yields.
[b] Ref. 4m.
[c] Ref. 11.
[d] Ref. 4g.
[e] Ref. 13.
[f] Ref. 4g.
[g] Ref. 12.
[h] Ref. 4a.
[i] Ref. 4f.