One-pot Synthetic Method of Allyl Sulfides: Samarium-induced Allyl Bromide Mediated Reduction of Alkyl Thiocyanates and Diaryl Disulfides in Methanolic Medium

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A convenient synthetic method of allyl sulfides by the treatment of alkyl thiocyanates or diaryl disulfides with Sm and allyl bromide in methanol has been developed.

The use of samarium diiodide as a single electron transfer reagent in organic synthesis has drawn chemist's attention. Numerous examples, such as coupling reduction, cyclization, and the Barbier reaction, have been widely reported.[1] Though SmI_2 is a useful reductive reagent, it is expensive. Furthermore, samarium diiodide is very sensitive to oxidation by air, so storage is difficult. Whereas metallic samarium is stable in air and has strong reducing power. Recently, it has been noted that cheaper and more convenient metallic samarium can be used directly as an alternative reductant of SmI_2 in organic synthesis.[2]

Because metallic samarium which is commercially available is not sufficiently reactive,[3] a lot of activating agents, such as I_2, HCl, $HgCl_2$, and TMSCl have been used to activate metallic samarium to mediate the reactions.[4] Recently, Banik B. K. reported that reductive coupling of aromatic ketones was achieved by samarium metal in the presence of allyl bromide.[5] Interestingly, no allylated product was obtained. Yet, when we used alkyl thiocyanates and diaryl disulfides as substrates in this system, allylated product was obtained. Herein we report that, by modifying the ratio of starting materials, allyl sulfides can be prepared efficiently in Sm/Allyl bromide/MeOH system.

We found that treatment with 3 equiv. of samarium metal and 3 equiv. of allyl bromide, alkyl thiocyanates were converted to allyl sulfides quickly and in good yields (Table 1, Entries1–5). When diaryl disulfides were treated with 5 equiv. of samarium metal and 6 equiv. of allyl bromide, we also got corresponding allyl sulfides in good yields (Entries 6–9). However, when we treated alkyl disulfides in this method, no allylated product or other reduced products were detected and only starting material recovered (Entry 10). Our experiment also showed that alkyl disulfides cannot be reduced to alkyl thiolates by SmI_2 at room temperature. In Entry 2, though TsO is a good leaving group, substrate was smoothly converted into corresponding allylated product with TsO group intact. Benzyl thiocyanate was allylated in 80% yield (Entry 3), yet, in $SmI_2/THF/H_2O$ system, benzyl thiocyanate was rapidly reduced to toluene owing to the strong reducing power of SmI_2. On the basis of the above results, we consider the Sm/Allyl bromide/MeOH system has a moderate reducing power.

In the process of exploring the role of allyl bromide, we found that in the absence of allyl bromide, no reaction was going on. When 0.6 equiv. of allyl bromide was used to mediate the reaction of $n\text{-}C_{16}H_{33}SCN$, ^1H NMR analysis of the crude product showed the ratio of $n\text{-}C_{16}H_{33}SCH_2CH{=}CH_2$:$n\text{-}C_{16}H_{33}SH$:$(n\text{-}C_{16}H_{33}S)_2$ was 37:58:5 (Entry 11), yet, when 3 equiv. of allyl bromide was used in this reaction, the ratio of $n\text{-}C_{16}H_{33}SCH_2CH{=}CH_2$:$n\text{-}C_{16}H_{33}SH$:$(n\text{-}C_{16}H_{33}S)_2$ was 92:7:1 (Entry 5), where allylated product was increased greatly. On the basis of the results in Table 1, we consider that allyl bromide might act as an activator of metalic samarium to mediate the reduction from alkyl thiocyanates to alkyl thiolates and alkyl disulfides.[6] In this process, allyl bromide was partially consumed to activate Sm, alkyl thiolate captured the remained allyl bromide and hence gave allylated product. Similarly, diaryl disulfides can also be reduced by activated Sm to aryl thiolates and allylated by allyl bromide.

$$RSCN \xrightarrow[\text{rt, 30min}]{\text{Sm/Allyl bromide/ MeOH}} RSCH_2CH{=}CH_2$$

$$ArSSAr \xrightarrow[\text{rt, 30min}]{\text{Sm/Allyl bromide/ MeOH}} ArSCH_2CH{=}CH_2$$

Scheme 1.

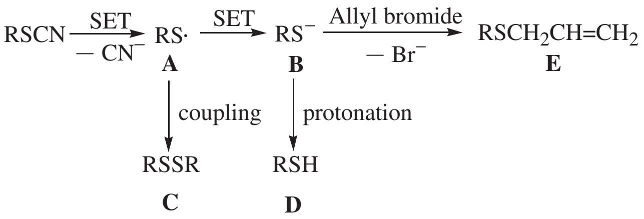
Table 1. Synthesis of allyl sulfides

Entry	Substrate	Molar Ratio (Substrate:Sm:Allyl Bromide)	Yield[a] of Allyl Product/%
1	$HO(CH_2)_6SCN$	1:3:3	91%
2	$TsO(CH_2)_6SCN$	1:3:3	93%
3	$PhCH_2SCN$	1:3:3	80%
4	$n\text{-}C_{12}H_{25}SCN$	1:3:3	84%
5	$n\text{-}C_{16}H_{33}SCN$	1:3:3	86%[b]
6	$(PhS)_2$	1:5:6	76%
7	$(p\text{-}MeC_6H_4S)_2$	1:5:6	80%
8	$(p\text{-}ClC_6H_4S)_2$	1:5:6	83%
9	$(p\text{-}BrC_6H_4S)_2$	1:5:6	81%
10	$(n\text{-}C_{16}H_{33}S)_2$	1:5:6	—[c]
11	$n\text{-}C_{16}H_{33}SCN$	1:3:0.6	30%[d]

[a] Isolated yield. [b] ^1H NMR analysis of the crude product was performed, the ratio of $n\text{-}C_{16}H_{33}SCH_2CH{=}CH_2$:$n\text{-}C_{16}H_{33}SH$:$(n\text{-}C_{16}H_{33}S)_2$ was 92:7:1. [c] No reaction, only starting material recovered. [d] ^1H NMR analysis of the crude product was performed, the ratio of $n\text{-}C_{16}H_{33}SCH_2CH{=}CH_2$:$n\text{-}C_{16}H_{33}SH$:$(n\text{-}C_{16}H_{33}S)_2$ was 37:58:5.

The possible mechanism for the reaction is proposed in Scheme 2. Taking $n\text{-}C_{16}H_{33}SCN$ as an example, it may involve the single-electron transfer (SET) process.

A single-electron transfer to alkyl thiocyanate firstly gives radical A. Subsequently, either self-coupling of radical A or further a single-electron transfer to radical A is feasible. As a result,



Scheme 2.

trace of disulfides C and a large amount of alkyl thiolate B are formed. Meanwhile, alkyl thiolate B can be protonated to generate the alkyl thiol D or more smoothly allylated by alkyl bromide to provide product E.

Table 2. Reactions of n-$C_{16}H_{33}SCN$ with samarium metal and allyl bromide in various protic solvent

Entry	Reaction Medium	Reaction Time	Yield of n-$C_{16}H_{33}SCH_2CH{=}CH_2$
1	MeOH	30 min	86%[a]
2	EtOH	45 min	31%[a]
3	*i*-PrOH	24 h	—[b]
4	*t*-BuOH	24 h	—[b]
5	THF/H_2O(10/1)	24 h	—[b]
6	MeOH/H_2O(10/1)	24 h	—[b]

[a] isolated yield. [b] no reaction, only starting material recovered.

We also attempted several other protic solvent as reaction medium in addition to MeOH. We found that using EtOH as reaction medium, the highest yield of allyl product we got was 31% (Table 2, Entry 2), and a prolonged reaction time did no service to yield. When secondary or tertiary alcohol was used in place of MeOH, even the mixture was stirred overnight, still no reduced product was detected, and there was only starting material recovered (Entries 3, 4). Although water as a protic solvent, efficaciously promotes the reductivity of SmI_2,[7] the action of Sm/Allyl bromide in the medium containing water was inert (Entries 5, 6).

The general procedure is as follows: At room temperature, to a mixture of samarium metal (1.5 mmol for alkyl thiocyanates or 2.5 mmol for diaryl disulfide) and substrate (0.5 mmol), allyl bromide (1.5 mmol for alkyl thiocyanate or 3 mmol for diaryl disulfide) was added under nitrogen. Subsequently, MeOH (8 mL) was added by a quick syringe. An exothermic reaction occurred, when MeOH was added. After 30 min, by TLC, the starting material was verified to have been consumed completely. The reaction mixture was diluted with 10 mL ethyl acetate, and was filtered through a small quantitative of silica gel. The filtrated solution was dried (Na_2SO_4) and then concentrated. For some cases, the ^1H NMR analysis of the crude products was performed. All crude products were purified by flash chromatography to yield the desired products.

In summary, a one-pot synthetic method of allyl sulfides by the treatment of alkyl thiocyanates or diaryl disulfides with Sm and allyl bromide in methanol has been developed. The notable advantages of this method are good yields, simple operation and neutral reaction conditions.

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