## Communications to the Editor

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# NOVEL ARYLTHIOMETHYLATION OF CARBONYL COMPOUNDS USING ARYLTHIOMETHYLTRIMETHYLSILANES CATALYZED BY FLUORIDE IONS. NEW ROUTE TO β-HYDROXYARYLSULFIDES[1]

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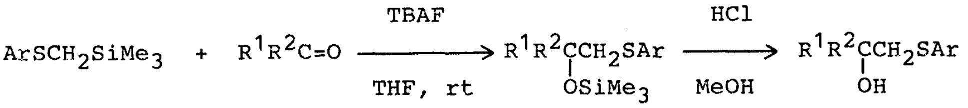
Arylthiomethyltrimethylsilanes are good and mild nucleophilic reagents for introducing arylthiomethyl groups into carbonyl compounds promoted by tetra-n-butylammonium fluoride to give the corresponding β-hydroxyarylsulfides in fairly good yields.

KEYWORDS ——— arylthio carbanion; fluoride ion-promoted alkylation; arylthiomethylation; β-hydroxyarylsulfide; arylthiomethyltrimethylsilane; chemoselective phenylthiomethylation

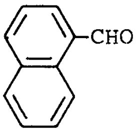
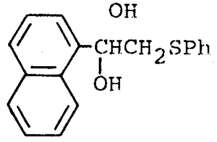
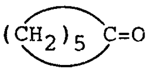
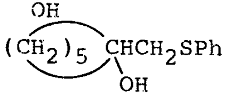
Organosulfur compounds are useful not only in organic synthesis, but also for their biological and pharmacological activities, and the introduction of organosulfur groups into carbon skeleton is one of the most important reactions in synthetic chemistry.[2] For this purpose, in general, α-thio carbanions, which are stabilized by the sulfur atom, are usually used.[3] In contrast with α-sulfinyl carbanion[4] and α-sulfonyl carbanion,[5] however, a combination of a strong lithium base and an activator such as DABCO, HMPA, or TMEDA is usually required for the generation of α-thio carbanion. Recently Takai and his coworkers have demonstrated new phenylthiomethylation by using chromium reagents.[6] In the extension of our studies on fluoride ion-promoted reactions of organosilicon compounds,[7] we have found that new access to α-arylthio carbanionic species can be readily attained by the reaction of arylthiomethyltrimethylsilane with fluoride ion, the results of which are the subject of this paper.[8] This provides a new entry to chemoselective arylthiomethylation of carbonyl compounds such as ketones and aldehydes to give the corresponding β-hydroxyarylsulfides (eq.1), which are known as versatile synthetic intermediates.[9]



$$\mathrm{ArSCH_2SiMe_3} + \mathrm{R^1R^2C{=}O} \xrightarrow[\text{THF, rt}]{\text{TBAF}} \mathrm{R^1R^2\underset{OSiMe_3}{\underset{|}{C}}CH_2SAr} \xrightarrow[\text{MeOH}]{\text{HCl}} \mathrm{R^1R^2\underset{OH}{\underset{|}{C}}CH_2SAr} \qquad (1)$$

**1a**, Ar = Ph **2** **3** **4**
**b**, Ar = $m$-$\mathrm{MeC_6H_5}$

Table I. Reaction of Arylthiomethyltrimethylsilane (**1**) with Carbonyl Compounds (**2**) Catalyzed by TBAF[a]

| Entry | Sulfide (**1**) | Carbonyl compound (**2**) | Product (**4**)[b] | % Yield[c] |
|---|---|---|---|---|
| 1 | $\mathrm{PhSCH_2SiMe_3}$ (**1a**) | PhCHO (**2a**) | $\mathrm{Ph\underset{OH}{C}HCH_2SPh}$ (**4a**) | 66 |
| 2 | **1a** | **2a** | **4a** | 96[d] |
| 3 | **1a** | $\mathrm{p\text{-}Me_2NC_6H_4CHO}$ (**2b**) | $\mathrm{p\text{-}Me_2NC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4b**) | 79 |
| 4 | **1a** | $\mathrm{p\text{-}MeOC_6H_4CHO}$ (**2c**) | $\mathrm{p\text{-}MeOC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4c**) | 66 |
| 5 | **1a** | $\mathrm{p\text{-}MeC_6H_4CHO}$ (**2d**) | $\mathrm{p\text{-}MeC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4d**) | 66 |
| 6 | **1a** | $\mathrm{p\text{-}ClC_6H_4CHO}$ (**2e**) | $\mathrm{p\text{-}ClC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4e**) | 51 |
| 7 | **1a** | $\mathrm{p\text{-}NCC_6H_4CHO}$ (**2f**) | $\mathrm{p\text{-}NCC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4f**) | 56[e] |
| 8 | **1a** | $\mathrm{p\text{-}O_2NC_6H_4CHO}$ (**2g**) | $\mathrm{p\text{-}O_2NC_6H_4\underset{OH}{C}HCH_2SPh}$ (**4g**) | 77[e] |
| 9 | **1a** | $\mathrm{PhCH_2CH_2CHO}$ (**2h**) | $\mathrm{PhCH_2CH_2\underset{OH}{C}HCH_2SPh}$ (**4h**) | 43 |
| 10 | **1a** | $\mathrm{Me(CH_2)_3CHO}$ (**2i**) | $\mathrm{Me(CH_2)_3\underset{OH}{C}HCH_2SPh}$ (**4i**) | 39 |
| 11 | **1a** |  (**2j**) |  (**4j**) | 79 |
| 12 | **1a** | PhCOMe (**2k**) | $\mathrm{Ph\underset{OH}{C}HMeCH_2SPh}$ (**4k**) | 35 |
| 13 | **1a** |  (**2l**) |  (**4l**) | 36 |
| 14 | $\mathrm{m\text{-}MeC_6H_4SCH_2SiMe_3}$ (**1b**) | **2a** | $\mathrm{Ph\underset{OH}{C}HCH_2SC_6H_4\text{-}m\text{-}Me}$ (**4m**) | 57 |

a) All reactions were carried out in the presence of 0.1 equivalent of TBAF in THF at rt for 15 h under argon, unless otherwise noted. b) Satisfactory spectroscopic data were obtained for all **4**. c) Yield after isolation by TLC. d) The 0.5 equivalent of TBAF was used. e) An equivalent of TBAF was used. Yield of **4g** was 20% when 0.1 equivalent of TBAF was used.

A general experimental procedure is given as the following. When phenylthiomethyltrimethylsilane[10] (**1a**, 0.6 mmol) was treated with carbonyl compounds (**2**, 0.5 mmol) such as aldehydes and ketones in the presence of a catalytic amount of tetra-n-butylammonium fluoride (TBAF, 0.05 mmol) in THF (3 ml) under argon, β-hydroxyphenylsulfides (**4**) were obtained in considerably high yield after acid methanolysis of the resulting silyl ethers (**3**). Overnight drying of TBAF-THF solution with molecular sieves 5A before the addition of the carbonyl compound into the reaction mixture is convenient and essential for improving the yield. Representative results are listed in Table I.

Some significant features of the present reaction are as follows: (1) Various aromatic and aliphatic substrates (**2**) can enter the reaction to give the corresponding β-hydroxyarylsulfides (**4**) under mild and almost neutral conditions. In particular, functional groups such as chloro, methoxy, nitro, amino, and cyano group are intact under the present conditions and chemoselective arylthiomethylation occurs. Moreover, m-tolylthiomethylation can be achieved by using **1b**. (2) The reaction proceeds smoothly for substrates bearing an electron-donating group on the aromatic ring rather than an electron-withdrawing substituent. Thus, although a catalytic amount of TBAF is sufficient for almost all **2**, the yield increases with increasing amounts of TBAF for several substrates that have lower reactivity. (3) The reaction proceeds via metal-free phenylthio carbanionic species. (4) Unexpectedly the relative reactivity of **1a** shows almost twice toward the reactivity of phenylthiomethyl(phenyldimethyl)-silane (**1c**).

In addition, the synthetic utility of the present reaction was mostly displayed by the ready accessibility of starting materials, easy manipulation of the conversion, and mild conditions.

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