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A Convenient Method for the Transformation of Alkenyl Sulfides to 2-(Phenylthio)alkanenitriles, Homoallyl Sulfides, and Thioacetals

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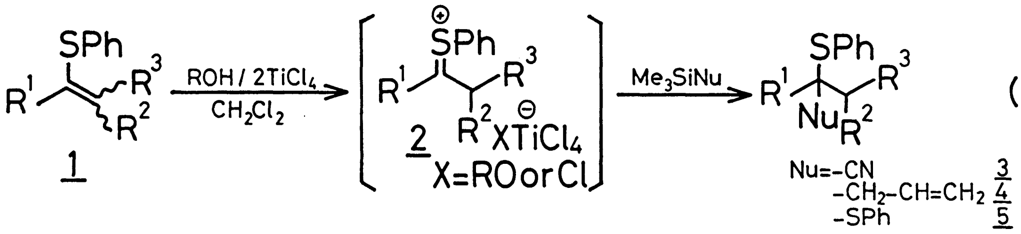
2-(Phenylthio)alkanenitriles, homoallyl sulfides, and thioacetals were obtained in good yields by the reaction of alkenyl sulfides with the corresponding silyl nucleophiles via thionium ion intermediates.

In the previous paper,$^{1)}$ we showed that the direct cross-aldol type reaction proceeded by the successive treatments of alkenyl sulfides (1) with the reagent prepared from $TiCl_4$ with an appropriate alcohol and trimethylsilyl enol ethers. This fact prompted us to investigate a new route to functionalized sulfides utilizing alkenyl sulfides as starting materials (Eq. 1).



(1)

First, we examined the synthesis of 2-(phenylthio)alkanenitriles (3), which were conventionally prepared by the sulfenation of alkanenitriles,$^{2)}$ the treatment of thioacetals with $Hg(CN)_2$ and iodine,$^{3)}$ or the reaction of thioacetals with trimethylsilyl cyanide in the presence of $SnCl_4$.$^{4)}$ The synthetic utility of 3 was recently demonstrated by Reetz and Starke.$^{4)}$ Further we reported a selective preparation of 2,2-dialkyl substituted alkanenitriles by the desulfurizative lithiation of 3 with tributylstannyllithium followed by the treatment with alkyl halides.$^{5)}$

Alkenyl sulfides were treated with a mixture of $TiCl_4$ and an alcohol (MeOH or t-BuOH) to form the corresponding thionium ion intermediates (2). Then 2 were allowed to react with trimethylsilyl cyanide to give 2-(phenylthio)alkanenitriles (3) in good yields (Table 1).

The following experimental procedure is representative; to a CH_2Cl_2 (1.1 ml) solution of $TiCl_4$ (2.2 mmol) was added a CH_2Cl_2 (1 ml) solution of methanol (1.1 mmol) at r.t. under argon and the reaction mixture was stirred for 1 h at the same temperature. 3-Phenylthio-2-pentene (178 mg, 1 mmol) in CH_2Cl_2 (2 ml) was added to the reaction mixture at -23 °C and the resulting deep red solution was stirred for 1 h. Then trimethylsilyl cyanide (1.5 mmol) was added and stirred for 2 h. The reaction mixture was quenched by addition of aqueous $NaHCO_3$ solution and the organic material was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and condensed under reduced pressure. The residue was chromatographed on silica gel (AcOEt-hexane) and 2-ethyl-2-(phenylthio)butanenitrile (195 mg) was isolated in 95% yield.

Table 1. Preparation of 2-(phenylthio)alkanenitriles (3)[a]

R^1	R^2	R^3	R	Time[b] h	Yield[6] %
$CH_3(CH_2)_7$	H	H	$(CH_3)_3C$	1	56
H	$CH_3(CH_2)_2$	H	CH_3	2	0
CH_3	CH_3	H	CH_3	1	70
			$(CH_3)_3C$	2	63
CH_3CH_2	CH_3	H	CH_3	2	95
$PhCH_2$	CH_3	H	CH_3	2	95
			$(CH_3)_3C$	2	68
$CH_3(CH_2)_7$	$Ph(CH_2)_2$	H	CH_3	2	67
			$(CH_3)_3C$	2	70
$-(CH_2)_4-$		H	CH_3	1	91
			$(CH_3)_3C$	1	40
CH_3	CH_3	CH_3	CH_3	2	58
			$(CH_3)_3C$	2	76
$-(CH_2)_4-$		CH_3	CH_3	2	80

a) All the reactions were performed with a similar procedure as described in the text, unless otherwise noted. b) The time for the reaction of 2 with $(CH_3)_3SiCN$.

Next, the reactions of allyltrimethylsilane and phenyl trimethylsilyl sulfide with alkenyl sulfides were examined under the similar reaction conditions. It was found that the corresponding homoallyl sulfides (4) and thioacetals (5) were also obtained in good yields by these reactions, respectively (Table 2). Concerning the preparation of homoallyl sulfides (4), the similar transformation such as the reaction of thioacetals with allylstannanes via thionium ions generated by the treatment of thioacetals with dimethyl(methylthio)sulfonium tetrafluoroborate was reported by Trost and Sato.[7] It is noted that the present transformation of alkenyl sulfide to homoallyl sulfide has an advantage that the reaction requires no specific reagent to generate the active intermediate. As to the preparation of thioacetals from alkenyl sulfides, the hydrogen chloride[8] and perchloric acid[9]

Table 2. Preparation of homoallyl sulfides (4) and thioacetals (5)a)

Me_3SiNu	R^1	R^2	R^3	Time b) / h	Yield 6) / %
$Me_3SiCH_2CH=CH_2$	$CH_3(CH_2)_7$	H	H	1	83
	CH_3CH_2	CH_3	H	1	81
	$CH_3(CH_2)_3$	$CH_3(CH_2)_2$	H	1	81
	$-(CH_2)_4-$		H	1	90
	CH_3	CH_3	CH_3	1	82
	$-(CH_2)_4-$		CH_3	1	85
Me_3SiSPh	CH_3	CH_3	H	2	73
	$-(CH_2)_4-$		H	2	75

a) The preparation of 2 was carried out at -23 °C for 1 h using MeOH. b) The time for the reaction of 2 with Me_3SiNu carried out at -78 °C.

promoted reactions of alkenyl sulfides with thiophenol were reported.

As shown in Table 1, 2-(phenylthio)alkanenitrile (3) possessing no alkyl substituent α to phenylthio group (R^1 = H) was not obtained by the present reaction owing to the instability of the corresponding thionium ion intermediate (2). The same is true for the reactions of allyltrimethylsilane and phenyl trimethylsilyl sulfide. Then an alternative route to those sulfides was explored. It was found that such 2-(phenylthio)alkanenitriles (7) were obtained when 1-(phenylthio)vinylsilanes (6), which were easily synthesized by the reaction of 1-(phenylthio)vinyllithium reagents with chlorotrimethylsilane,10) were employed as starting materials. On the other hand, trimethylsilyl group of the products was not hydrolyzed during the usual workup and the corresponding α-trimethylsilyl homoallyl sulfides and thioacetals (8) were isolated in good yields by the reactions of allyltrimethylsilane and phenyl trimethylsilyl sulfide with 6 (Eq. 2, Table 3).

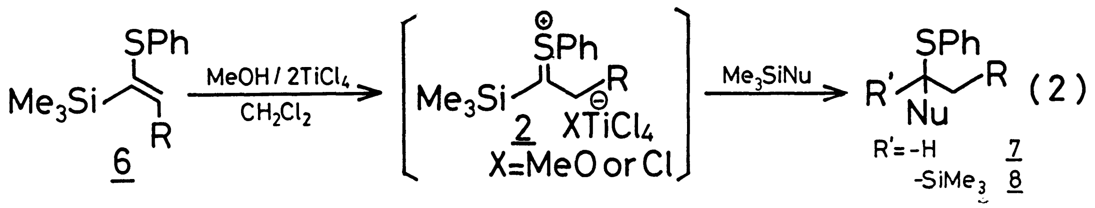


Table 3. Reaction of 1-(phenylthio)vinylsilanes (6) with the silyl nucleophiles

R	Me_3SiNu	Time[a)] h	Temp[b)] °C	Time[b)] h	Product	Yield[6)] %
CH_3CH_2	Me_3SiCN	1	-23	2.5	7	78
	$Me_3SiCH_2CH=CH_2$	2	-78	1	8	65
$CH_3(CH_2)_6$	Me_3SiCN	2	-23	2.5	7	78
	$Me_3SiCH_2CH=CH_2$	2.5	-78	1	8	63
	Me_3SiSPh	2	-78	2	8	70
$(CH_3)_2CH$	Me_3SiCN	2	-78	2	7	67
	Me_3SiSPh	2	-78	2	8	80

a) The reaction time for the preparation of 2 carried out at -23 °C using MeOH. b) The conditions of the reaction of 2 with Me_3SiNu.

Since alkenyl sulfides are easily prepared by the various reactions and starting materials,[11)] it should be noted that the present method provides a useful synthetic route to functionalized sulfides.

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