

REACTION OF β -PHENYLTHIOALKYL TITANIUM REAGENTS
WITH CARBONYL COMPOUNDS

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β -Phenylthioalkyltitanium reagent prepared by the hydrotitanation of alkenyl sulfide using triethylsilane and titanium tetrachloride is found to react with aromatic aldehyde or α, β -unsaturated ketone to give the corresponding γ -hydroxyalkyl sulfide or δ -phenylthio ketone, respectively.

Recently, much attention have been paid on the synthetic utility of alkyltitanium reagents because of their stereo and functional group selectivity observed in the reaction with carbonyl compounds¹⁾.

In the previous paper²⁾, we showed that the reduction of alkenyl sulfide (1) with triethylsilane in the presence of titanium tetrachloride gave β -phenylthioalkyltitanium compound (2) which is regarded as an unusual " β -thio carbanion". This report summarizes the results of the study on the reaction of the titanium reagent (2) with aldehydes and ketones.

First, the reaction of 2 with aromatic aldehyde was examined. When the titanium reagent (2) prepared by the hydrotitanation of 2-phenylthio-2-butene (1) was allowed to react with benzaldehyde at -78°C , the γ -hydroxy sulfide (3) was produced in 70% yield. Further it was found that addition of zinc bromide increased the yield of the product (3). In a similar manner, the reactions of 2 with several substituted benzaldehydes were performed and the corresponding adducts (3) were obtained in good to moderate yields (Eq-1, Table-1).

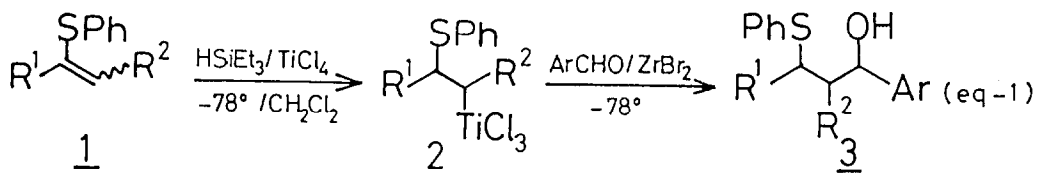

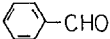
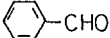
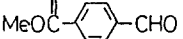
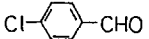
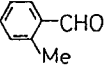
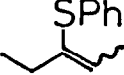
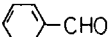
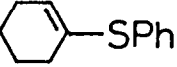
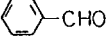
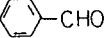


Table 1. Reaction of the titanium reagents (2) with aromatic aldehydes.^{a)}

Alkenyl Sulfide	ArCHO	Time (h)	Yield (%) ^{b)}
		1.5	70 ^{c)}
		1.5	77
		1	73
		1.3	72
		1	78

		1.5	53

		1	47 ^{c)}
		1	55

a) All the reactions were carried out by a similar procedure to that described for the reaction with α,β -unsaturated ketones. Ratio of 1/ Et₃SiH/ TiCl₄/ ZnBr₂/ ArCHO = 1: 1.1: 1.1: 1.2: 1.2. b) All the products were identified by IR and NMR spectra. c) In the absence of ZnBr₂.

On the other hand, unsuccessful result was obtained when aliphatic aldehyde or aromatic ketone was employed. In such a case, unreacted alkyl sulfide was isolated as a major product along with a small amount of starting alkenyl sulfide. It was also confirmed that aliphatic ketone was unreactive in the reaction of 2 under a similar reaction conditions.

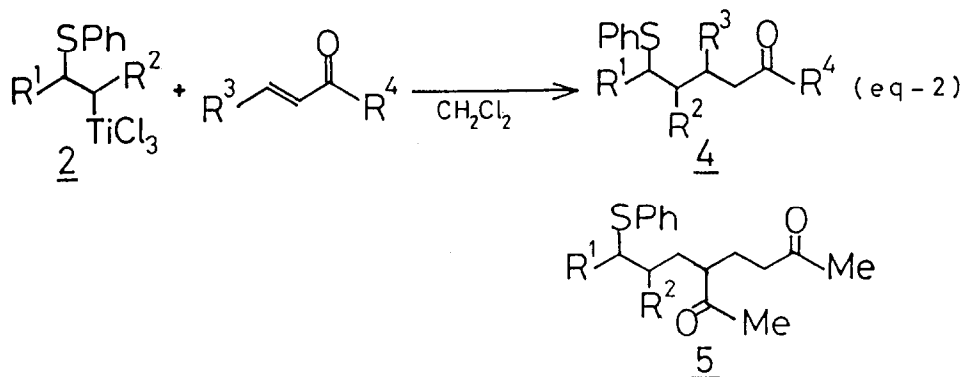
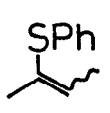
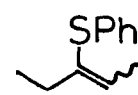
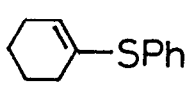
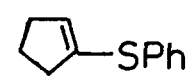


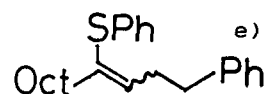
Table 2. Reaction of the titanium reagents (2) with α,β -unsaturated ketones

Alkenyl Sulfide	R ³	R ⁴	Temp (°C)	Time (h)	Yield ^{b)} (%)
	Ph	CH ₃	-78	2	76 ^{c)}
	H	CH ₃	-48	4	52 (10) ^{d)}
	CH ₃	CH ₃ (CH ₂) ₇	-48	4	63 ^{c)}
	-(CH ₂) ₃ -		-78	3	72 ^{c)}

	Ph	CH ₃	-78	3	70 ^{c)}
	H	CH ₃	-48	4	32 (31) ^{d)}
	CH ₃	CH ₃ (CH ₂) ₇	-48	4	66 ^{c)}

	Ph	Ph	-78	3.5	77 ^{c)}
	H	CH ₃	-48	4	45 (21) ^{d)}
	CH ₃	CH ₃ (CH ₂) ₇	-48	4	70
	-(CH ₂) ₃ -		-78	5	62 ^{c)}

		-(CH ₂) ₃ -	-78	4	64 ^{c)}

	e) H	CH ₃	-48	4	48 (25) ^{d)}
	CH ₃	CH ₃ (CH ₂) ₇	-48	4	53 ^{c)}

a) All reactions were performed with a same procedure as described in the text, unless otherwise noted. b) All products were identified by IR and NMR spectra. c) 1.05 equiv of α,β -unsaturated ketone were used. d) Yield of 5. e) Alkenyl sulfide was treated with Et₃SiH/TiCl₄ for 1 h.

Next, α,β -unsaturated ketone was subjected to the reaction with the titanium reagent (2). In contrast to the above result, it was found that the Michael adduct (4) was produced in good yield. The selectivity of the present reaction is excellent and the formation of 1,2-adduct was not observed (Eq-2).

The typical experimental procedure for the Michael reaction of 2 with α,β -unsaturated ketone is as follows; to a CH_2Cl_2 (4 ml) solution of triethylsilane (128 mg, 1.1 mmol) and 1-(phenylthio)cyclohexene (191 mg, 1 mmol) was added a CH_2Cl_2 solution of titanium tetrachloride (1.1 mmol) at -78°C and the reaction mixture was stirred for 30 min. A CH_2Cl_2 (1 ml) solution of 2-dodecen-4-one (273 mg, 1.5 mmol) was added to the resulting deep red solution of the alkyltitanium reagent (2) at -78°C and the reaction mixture was warmed up to -48°C . After stirring for 4 h at the same temperature, the reaction was quenched by addition of water. The organic material was extracted with CH_2Cl_2 and the extract was dried over Na_2SO_4 . After evaporation of the solvent, the residue was chromatographed on silica gel (AcOEt-hexane) and 2-[2-(phenylthio)cyclohexyl]-4-dodecanone (4) (262 mg) was isolated in 70% yield.

As shown in Table 2, the various δ -phenylthio ketones (4) can be synthesized in good yields by way of β -phenylthioalkyltitanium reagents (2). When methyl vinyl ketone was employed as an acceptor, the considerable amount of 1,5-diketone (5) was isolated as a by-product. The formation of 5 was apparently due to the further reaction of the initially formed titanium enolate with methyl vinyl ketone.

Further study on the reaction of alkyltitanium compound (2) is now in progress.

References

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- 2) T. Takeda, T. Tsuchida, and T. Fujiwara, *Chem. Lett.*, 1984, 1219.

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