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REGIO AND STEREOSELECTIVE COUPLING REACTION OF GRIGNARD REAGENTS WITH β-PHENYLTHIO β,γ-UNSATURATED ALCOHOLS USING TETRACHLOROSILANE. A NEW METHOD FOR THE PREPARATION OF (Z)-ALKENYL SULFIDES

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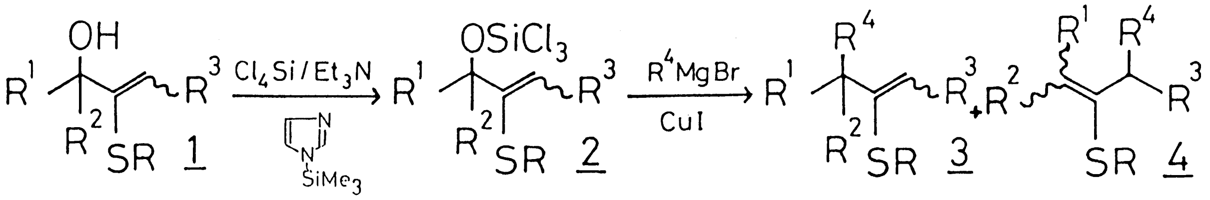
The coupling reaction of (E)-β-phenylthio β,γ-unsaturated alcohols with Grignard reagents using tetrachlorosilane as a condensation reagent gave (Z)-S_N2' products exclusively, whereas the reaction of the corresponding Z-isomers proceeded by S_N2 attack with retention of double bond geometry.

Although various methods for the synthesis of alkenyl sulfides have been studied, the stereoselective preparation is still a problem awaiting solution. Concerning the synthesis of (E)-1,2-disubstituted vinyl sulfides, Takei et al. reported that the alkylation of 1-(phenylsulfinyl)vinyllithium reagents followed by the reduction gave (E)-alkenyl sulfides.1) We also reported that (E)-alkenyl sulfides were obtained by the reaction of some electrophiles with 1-(phenylthio)vinyllithium reagents prepared from 2-methoxyalkyl sulfides.2) However, practical method for the preparation of (Z)-alkenyl sulfide have not been studied yet.3)

In this communication, we wish to describe a new method for the preparation of (Z)-alkenyl sulfides by the regio and stereoselective coupling reaction of β-phenylthio β,γ-unsaturated alcohols (1) with Grignard reagents.

In general, the coupling reaction of allylic alcohols with organometallics is performed by two-step procedure via the corresponding halides, esters, ethers, carbonates, or tosylates.4) The more convenient method is single-step transformation of allylic alcohol itself or one-pot conversion via the appropriate derivatives, prepared in situ. Various reagents including nickel catalyst,5) N-methyl-N-phenylaminophosphonium iodide,6) 2-fluoropyridinium salt,7) or α-chloroenamines8) have been developed for this purpose. A simple one-step transformation using alkylcopper-Lewis acid was also reported.9) We found that commercially available and inexpensive tetrachlorosilane was an effective condensation reagent.

The allylic alcohols (1) were treated with tetrachlorosilane in the presence



of triethylamine and a catalytic amount of N-trimethylsilylimidazole in THF to give the corresponding trichlorosilyl ethers (2), which could be isolated by distillation.[10] First, we examined the reaction of trichlorosilyl ethers (2a,b,c), which had no γ-substituent. The trichlorosilyl ether (2a) was allowed to react with excess Grignard reagents in THF at r.t. and the coupling products (3 and 4) were obtained in 50% yield (run 1). Addition of copper(I) iodide increased the yield and the ratio of S_N2' product (4)(run 2). However, the stereochemical purity of the S_N2' product was found to be insufficient (run 3). As expected, the S_N2' product (4) was exclusively produced when the tertiary substrate was employed (run 5). It was noteworthy that the comparable result was achieved by the one-pot reaction which was carried out by the successive addition of copper (I) iodide and Grignard reagent to the reaction mixture after the trichlorosilyl ether (2) was prepared (runs 4,6).

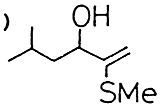
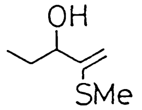
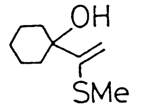
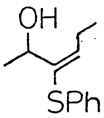
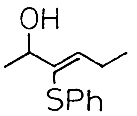
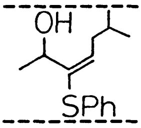
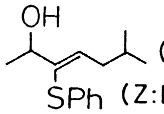
What is striking is a fact that the regiochemistry of the reaction of the β-phenylthio β,γ-unsaturated alcohols possessing a γ-substituent (1d and e) depends on their geometry of the double bond. Further, it was found that (Z)-alkenyl sulfides were exclusively produced from both E- and Z-1 and the stereochemical purity of S_N2 and S_N2' products of the present reaction was extremely high (>98%). For example, the one-pot reaction of (E)-3-phenylthio-3-hexen-2-ol (1d) with octylmagnesium bromide at r.t. gave the (Z)-S_N2' product (4) with 97% selectivity along with a small amount of (Z)-S_N2 product (3) (run 8). On the other hand, the corresponding Z-isomer[11] was found to react with the Grignard reagent at -78 °C to the product of (Z)-S_N2 attack (86% selectivity) (run 15). Since the starting material contained 4% of E-isomer, the corrected value of the selectivity was 89% (Table 1).

The typical experimental procedure for the one-pot reaction is as follows; to a THF (6 ml) solution of triethylamine (0.21 ml, 1.5 mmol), tetrachlorosilane (0.17 ml, 1.5 mmol) and a catalytic amount of N-trimethylsilylimidazole was added dropwise a THF (4 ml) solution of (E)-3-phenylthio-3-hexen-2-ol (1d) (208 mg, 1 mmol) at -18 °C. Then the reaction mixture was gradually warmed up to r.t. After stirring for 4.5 h, CuI (57 mg, 0.3 mmol) and a THF solution of octylmagnesium bromide (6mmol) were subsequently added and stirred for 40 min. The reaction was quenched by addition of aqueous NH_4Cl solution. The organic layer was extracted with AcOEt and dried over Na_2SO_4. After removal of the solvent, the residue was chromatographed on silica-gel TLC (hexane) to give a mixture of (Z)-4ethyl-3-phenylthio-2-dodecene (4) and (Z)-5-methyl-4-phenylthio-3-tridecene (3) (245 mg) in the ratio of 97:3 in 80% yield.

Concerning the coupling reaction of β-phenylthio β,γ-unsaturated alcohol derivatives with organometallic compounds, Trost and Tanigawa reported that the reaction of the cyclic acetates with cuprates proceeded by S_N2 process.[13] Then, we examined the regio and stereochemistry of the reaction of the acyclic acetates (5) with cuprates. The coupling reaction was carried out in THF at -50 °C for 1 h and it was found that the regio and stereochemistry of the reaction was identical with those of the reaction of the trichlorosilyl ether with the Grignard reagent (Table 2).

Since the phenylthio group of alkenyl sulfide can be reductively removed[14] or replaced by alkyl group[1] with retention of configuration, the present reaction

Table 1. The one-pot coupling reaction of the β-phenylthio β,γ-unsaturated alcohol[a]

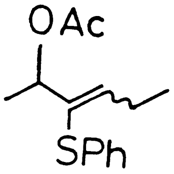
Run		R^4	Temp/°C	Yield/%	Ratio of product[e] E-3:Z-3:E-4:Z-4
1[b,c]	 1a	Phenyl	r.t.	50	17 : 83[f,g]
2[b]		Phenyl	r.t.	84	8 : 92[f,g]
3[b]	 1b	Octyl	r.t.	61	19 : 32: 49[f]
4		Octyl	r.t.	56	13 : 31: 56[f]
5[b]	 1c	Butyl	r.t.	75	<5 : >95[f]
6		Butyl	r.t.	74	<5 : >95[f]
7[b]	 (E)-1d	Octyl	r.t.	89	<1: 4: <1: 96
8		Octyl	r.t.	80	<1: 3: <1: 97
9		Octyl	-78-r.t.	87	<1: 5: <1: 95
10		Butyl	r.t.	76	<1: 2: <1: 98
11		Ethyl	r.t.	70	<1: 2: 2: 96
12[b]	 (Z)-1d (Z:E=96:4)	Octyl	r.t.	73	<1: 80: <1: 20
13[b,d]		Octyl	r.t.	51	<1: 65: <1: 35
14		Octyl	r.t.	63	<1: 67: <1: 33
15		Octyl	-78-r.t.	76	<1: 86: <1: 14
16		Butyl	-78-r.t.	75	<1: 86: <1: 14
17		Ethyl	-78-r.t.	53	<1: 81: <1: 19
18	 (E)-1e	Octyl	r.t.	74	<1: 1: 1: 98
19	 (Z)-1e (Z:E=96:4)	Octyl	-78-r.t.	76	<1: 90: <1: 10

a) All reactions were performed with a same procedure as described in the text, unless otherwise noted. b) The reaction was carried out using the corresponding isolated trichlorosilyl ether (2). c) The reaction was carried out without CuI. d) One point one equiv. of Grignard reagent were used. e) Determined by HPLC analysis (Merck Si 60; solvent, Hexane-AcOEt (95:5)) after alkenyl sulfides (3 and 4) were converted to the corresponding sulfones. The oxidation was carried out by the treatment with MCPBA (2.5 equiv.) in CH_2Cl_2 at 0 °C and the sulfones were obtained in >95% yields. All products were identified by IR and NMR spectra and comparison with authentic alkenyl sulfides (mixture of stereoisomers) prepared according to the procedure of Corey and Shulman[12] by HPLC. f) Determined by NMR spectrum. g) Mixture of stereoisomers.

provides a convenient method for the regio and stereoselective preparation of olefinic compounds.

Table 2. The coupling reaction of the acetate (5) with lithium dialkylcuprates

Substrate	R^4	Yield/%	Ratio of products E-3:Z-3:E-4:Z-4
E-5	Octyl	74	<1: 6: <1: 94
	Butyl	79	<1: 8: <1: 92
Z-5 (Z:E = 96:4)	Octyl	71	<1: 88: <1: 12
	Butyl	73	<1: 89: <1: 11



5

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10) The yields and boiling points of the isolated trichlorosilyl ethers (2) were as follows; 2a (45%, 101-104 °C/6 mmHg), 2b (47%, 96-98 °C/10 mmHg), 2c (43%, 102-106 °C/0.5 mmHg), (E)-2d (51%, bp 116-118 °C/0.7 mmHg), (Z)-2d (58%, 103-105 °C/0.4 mmHg). (1 Torr= 133.322 Pa)

11) We found that (Z)-β-phenylthio β,γ-unsaturated alcohols (1) were stereoselectively prepared by the photoisomerization of (E)-1. The experimental procedure for the preparation of (Z)-1d was as follows; a hexane (80 ml) solution of (E)-1d (20 mmol) and acetophenone (1 mmol) in a Pyrex test tube was irradiated with a 400 W high pressure mercury lamp for 18 h. After evaporation of the solvent, the crude alkenyl sulfide was purified by distillation and (Z)-1d was obtained in 70% yield. The ratio of isomers (Z:E = 96:4) was determined by HPLC (Merck Si 60; solvent hexane-AcOEt (97.5:2.5) for the corresponding acetate. In a similar manner, (Z)-1e (Z:E = 96:4) was obtained in 65% yield from (E)-1e. In contrast with the above result, the irradiation of (E)-1,2-dialkyl substituted vinyl sulfide gave only an almost 1:1 mixture of the stereoisomers.

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