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A CROSS-ALDOL TYPE REACTION OF ALKENYL SULFIDE WITH TRIMETHYLSILYL ENOL ETHER.

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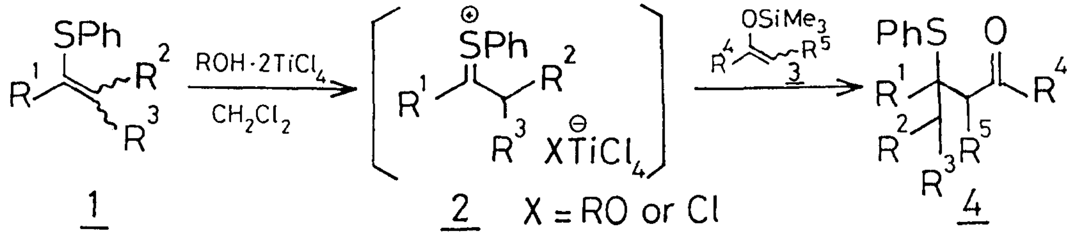
β-Phenylthio ketones were obtained in good yields by the successive treatment of alkenyl sulfides with $TiCl_4$-ROH (R= Me or t-Bu) and trimethylsilyl enol ethers.

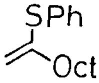
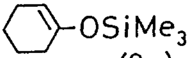
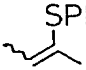
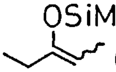
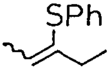
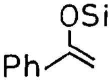
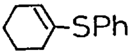
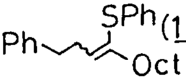
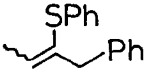
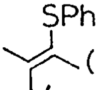
Alkenyl sulfides are regarded as "masked carbonyl compounds" and various methods for the preparation of them including the alkylation of 1-(alkylthio)vinyllithium reagents were reported.[1)] Although several reagents are developed for the hydrolysis of alkenyl sulfides to the corresponding carbonyl compounds,[2)] it is well known that alkenyl sulfides are rather unsusceptible to hydrolysis as compared with other masked carbonyl compounds such as thioacetals. Therefore, it is important to investigate their direct reactions with nucleophilic reagents to extend the application of alkenyl sulfides in organic synthesis. In this communication, we wish to describe a simple procedure for a cross-aldol type reaction of alkenyl sulfides (1) with trimethylsilyl enol ethers (3).



Alkenyl sulfides (1) were treated with the reagent prepared by addition of one equiv. of alcohol to two equiv. of $TiCl_4$ to produce intermediates which are suggested to be the thionium ions such as 2.[3)] When the thionium ion intermediates (2) were allowed to react with trimethylsilyl enol ethers, β-phenylthio ketones (4), which correspond to β-hydroxy ketones in normal cross-aldol reactions, were produced in good yields.

The reaction procedure is operationally simple as being illustrated by a typical example; To a CH_2Cl_2 (1.1 ml) solution of $TiCl_4$ (2.2 mmol) was added a CH_2Cl_2 (1.1 ml) solution of MeOH (1.1 mmol) at r.t. After stirring for 1 h at the same temperature, 2-phenylthio-2-butene (164 mg, 1 mmol) in CH_2Cl_2 (2 ml) was added to the reaction mixture at -23 °C and

Table. Cross-aldol type reaction of alkenyl sulfide (1) with trimethylsilyl enol ether (3)[a)]

Alkenyl Sulfide	Trimethylsilyl Enol Ether	ROH	Temp °C	Time[b)] h	Yield[c)] %	Ratio of Stereoisomers[d)]
 (1a)	 (3a)	MeOH	-23	1.5	65	
 (1b)	3a	MeOH	-23	1.5	87	
1b	 (3b)	MeOH	-23	1.5	81	60 : 40
 (1c)	 (3c)	MeOH	-23	1.5	76	
1c	3c	t-BuOH	-78	2.5	45	
 (1d)	3a	MeOH	-23	1.5	87	
1d	3b	MeOH	-23	1.5	79	
1d	3c	MeOH	-23	1.5	61	
 (1e)	3c	t-BuOH	-78	3	59	
 (1f)	3a	t-BuOH	-78	3	57	55 : 45
 (1g)	3b	MeOH	-23	1.5	56	57 : 43
 (1h)	3c	MeOH	-23	1.5	46	
1h	3c	t-BuOH	-78	3	57	

a) All reactions were performed with a same procedure as described in the text, unless otherwise noted. b) Conditions of the reaction of 2 with trimethylsilyl enol ether (3). c) All products were identified by IR and NMR spectra. d) Determined by HPLC analysis (Merk Si 60; solvent, hexane-AcOEt (9:1)) after β-phenylthio ketones (4) were converted to the corresponding sulfones with MCPBA (2.5 equiv.) in CH_2Cl_2.

the mixture was stirred for 1 h. Then 3-trimethylsiloxy-2-pentene (190 mg, 1.2 mmol) in CH_2Cl_2 (2 ml) was added and stirring was continued for 1.5 h. The reaction was quenched by addition of water 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 (hexane - AcOEt) and 4,5-dimethyl-5-(phenylthio)heptan-3-one (202 mg) was isolated in 81% yield.

In a similar manner, various β-phenylthio ketones (4) were obtained from alkenyl sulfides possessing an alkyl group at the position α to phenylthio group (1) ($R^1 \neq H$) as shown in the Table. In contrast with the above results, the reaction was complicated and β-phenylthio ketone (4) was not isolated when 2-monoalkyl substituted vinyl sulfide (1) ($R^1 = H$) such as 1-(phenylthio)-1-nonene was employed. It is assumed that the complication of the reaction is due to the instability of the thionium ion intermediate.

Recently, several methods for the generation of thionium ions such as the reaction of α-chloro sulfide with Lewis acid,4) the treatment of thioacetal with dimethyl(methylthio)sulfonium tetrafluoroborate,5) or the activation of thioacetal with trityl tetrafluoroborate6) were reported. It should be noted that the treatment of alkenyl sulfides with $TiCl_4$-ROH provides a simple and convenient method for the generation of such an active intermediates.

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3) It is assumed that hydrogen chloride is partially formed when alcohol is added to a CH_2Cl_2 solution of $TiCl_4$. Concerning the reaction of hydrogen chloride with alkenyl sulfide, it was reported that the treatment of 2-substituted vinyl sulfide ($C_5H_{11}CH{=}CHSPh$) with hydrogen chloride in benzene gave the corresponding α-chloro sulfide.a) On the other hand, Caserio et al. noted that hydrochlorinated product is unstable and was not obtained by the reaction of hydrogen chloride with alkenyl sulfide possessing an alkyl substituent at the position α to alkylthio group

($CH_2=C(CH_3)SPh$). They also noted that the formation of α-chloro sulfide was observed by NMR only when 2-(methylthio)propene was treated with a catalytic amount of hydrogen chloride.[b) a) A. J. Mura, Jr., G. Majetich, P. A. Grieco, and T. Cohen, Tetrahedron Lett., 1975, 4437; b) J. K. Kim, J. K. Pau, abd M. C. Caserio, J. Org. Chem., 44, 1544 (1979).

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