

## $\alpha$ -silyl carbonyl compounds

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**Abstract** - The chemistry of  $\alpha$ -silyl carbonyl compounds with an emphasis on the developments coming from the direct C-silylation of ester enolates with methyldiphenylchlorosilane is discussed. Several of the synthetic applications of the  $\alpha$ -silyl carbonyl systems are considered.

### INTRODUCTION

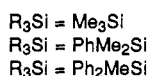
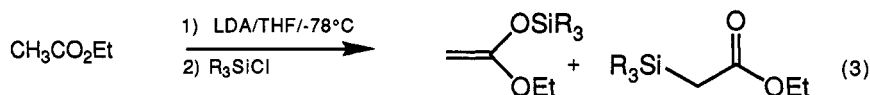
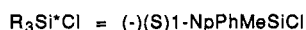
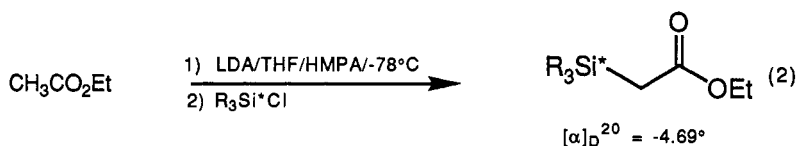
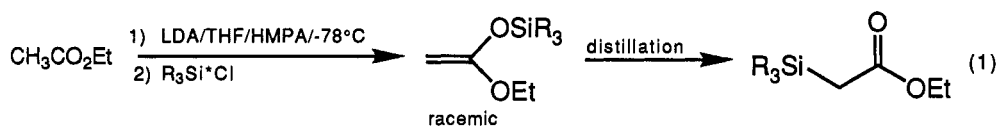
The chemistry of  $\alpha$ -silyl carbonyl compounds dates back some three decades when they were prepared, but were not much studied, especially in a synthetic sense. In the sixties several spectral studies on these materials were reported and their rearrangement to silyl enol ethers studied. No real synthetic uses of the  $\alpha$ -silyl carbonyl compounds were investigated until the early 1980's after the general interest in organosilanes as new and novel synthetic reagents had been established. It is the purpose of this paper to provide a partial review of the chemistry of  $\alpha$ -silyl carbonyl esters and ketones with an emphasis on the contributions from the author and his group.

### SYNTHESIS

There are now several syntheses of  $\alpha$ -silyl compounds in the literature. Among the more general are oxidation of  $\beta$ -hydroxysilanes (ref. 2), reaction of  $\alpha$ -silyl organometallic reagents with acid chlorides (ref. 3), or esters (ref. 4), the insertion of carbenes or carbenoids into the silicon-hydrogen bond (ref. 5), the silylation of certain ester enolates (ref. 6), but not enolates of ketones or aldehydes (ref. 7), and the reaction of esters or lactones with trimethylsilyl trifluoromethane sulfonate (ref. 8). The direct silylation of carboxylic acid dianions provides  $\alpha$ -silyl carboxylic acids (ref. 9). Rearrangements of various kinds also lead to  $\alpha$ -silyl ketones (refs. 10-13), in one noteworthy process a rearrangement directly from the readily available enol silyl ether to an  $\alpha$ -silyl ketone is possible (ref. 10).

Our own involvement in the chemistry of  $\alpha$ -silyl carbonyls came from an interest in studying the synthetic potential of the silyl ketene acetal derived from ethyl acetate and (S)(-) 1-naphthylphenylmethylchlorosilane ( $R_3Si^*Cl$ ). Treatment of the lithium enolate of ethyl acetate with the optically active silane in tetrahydrofuran/hexamethylphosphoric triamide gave racemic silyl ketene acetal, which upon distillation rearranged to the C-silylated material. (eq. 1) Running the reaction in the absence of hexamethylphosphoric triamide, which is known to catalyze the racemization of optically active chlorosilanes, provided the C-silylated material, (R)(+) ethyl (1-naphthylphenylmethyl)acetate in excellent yield and complete inversion at silicon (ref. 7). (eq. 2) These results are contrary to those found when trialkylchlorosilanes are employed in the reaction with ester enolates (ref. 14) and it was therefore decided to investigate the effect of aryl groups on the regiochemistry of silylation of ester enolates (ref. 15). Indeed, when the ester enolate is silylated with trimethylchlorosilane the O-silylated product is almost always the major, if not sole, product. When the enolate of ethyl acetate was quenched with dimethylphenylchlorosilane a mixture of O- and C-silylated products was obtained. However, when methyldiphenylchlorosilane was used to quench the enolate only the C-silylated product was observed. (eq. 3) All of these reactions are in tetrahydrofuran as solvent since in the presence of hexamethylphosphoric triamide O-silylation is enhanced. This phenomenon was further found to apply to  $\alpha$ -

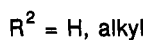
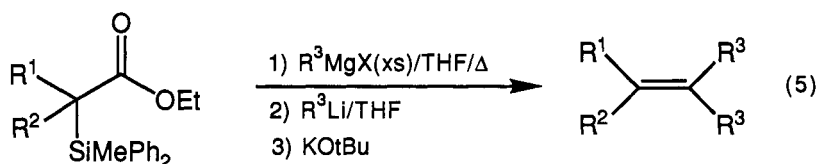
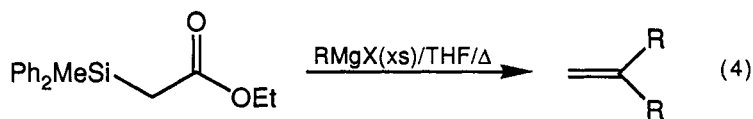
substituted esters and to  $\gamma$ -lactones, but not well to  $\alpha,\alpha$ -disubstituted esters or to  $\alpha$ -substituted lactones (ref. 15). It is, however, possible to prepare these materials *via* alkylation of the  $\alpha$ -silyl esters or lactones.

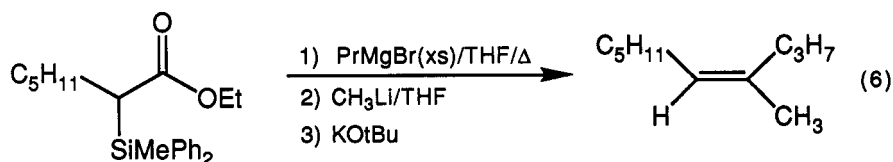


## SYNTHETIC APPLICATIONS

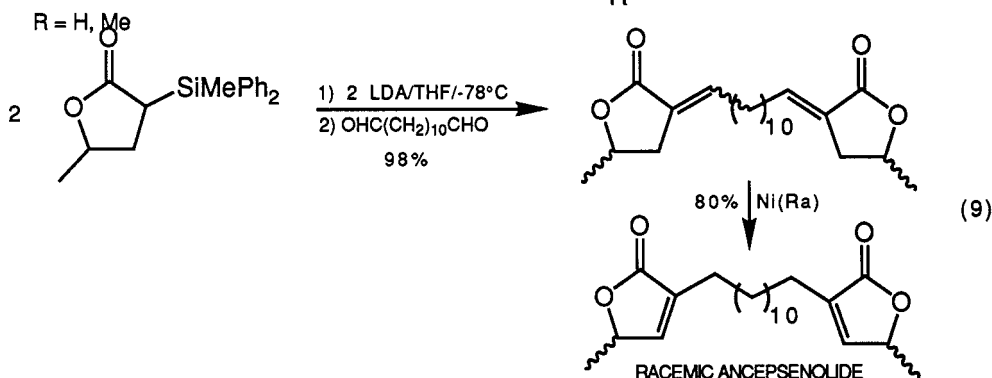
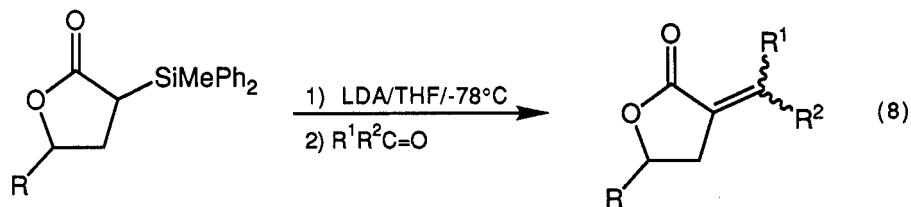
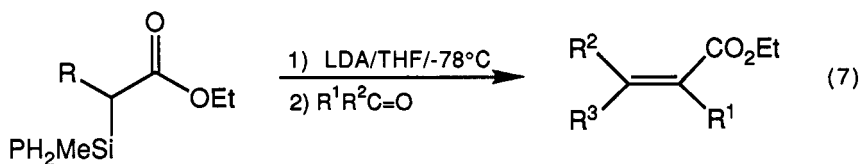
### Preparation of olefins

The reaction of  $\alpha$ -silyl ketones (ref. 16) and  $\alpha$ -silyl aldehydes (ref. 17) have been reacted with Grignard reagents to give olefins either directly or after elimination of the  $\beta$ -hydroxysilane. Thus, these  $\alpha$ -silyl carbonyls can be considered as vinyl cation equivalents. The reaction of Grignard reagents with ethyl trimethylsilylacetate on the other hand was reported to give a synthetically useless mixture of products (ref. 18). We found that for the successful reaction of  $\alpha$ -methyl diphenylsilyl esters with Grignard reagents absolutely pure magnesium for the preparation of the Grignard reagent is essential (ref. 19). The reaction of  $\alpha$ -methyl diphenylsilyl esters with organolithium reagents on the other hand gives a synthetically useless product mixture. Thus for the reaction of  $\alpha$ -silyl esters with Grignard reagents they can be considered as 1,1-vinyl dication equivalents. The addition of two equivalents of a Grignard reagent to an  $\alpha$ -methyl diphenylsilyl ester is only successful when an unsubstituted ester (i.e. an acetate) is employed and is therefore, only useful in the preparation of 1,1-disubstituted ethylenes (ref. 19). (eq. 4) It was discovered that it is possible to react an  $\alpha$ -alkyl (or  $\alpha,\alpha$ -dialkyl)- $\alpha$ -(methyl diphenylsilyl) ester with first a Grignard reagent and then an organolithium reagent to provide tri- and tetrasubstituted olefins in moderate to good yields (ref. 20). (eq. 5) In one case a stereospecific synthesis of a trisubstituted olefin was accomplished in a two-step, single flask operation. (eq. 6) It was found, however, that ethyl 2-(methyl diphenylsilyl)-3-butenate can be reacted with two equivalents of a Grignard reagent to give the corresponding 1,3-diene in moderate yields (ref. 21).



 **$\alpha,\beta$ -Unsaturated esters and lactones**

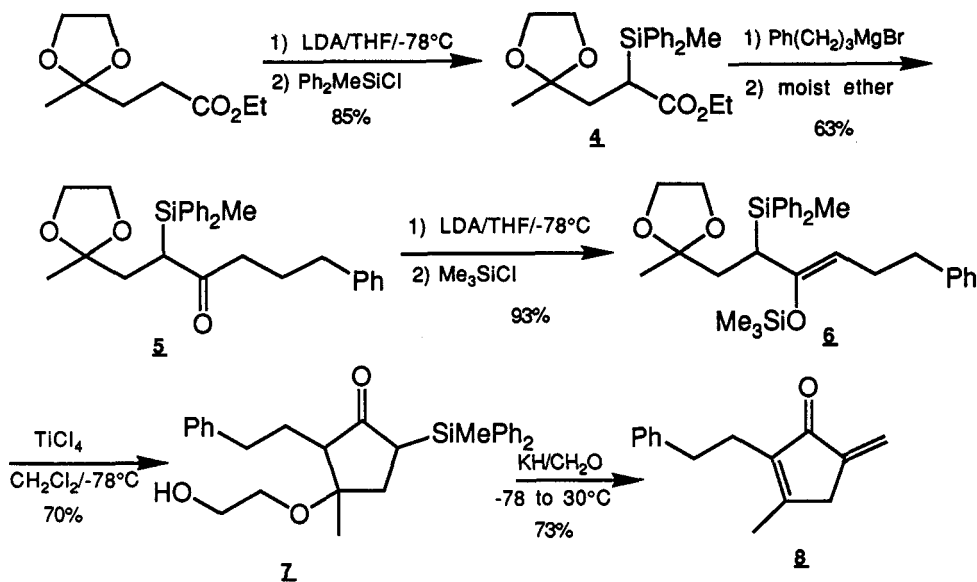
Although the reaction of the lithium enolate of unsubstituted  $\alpha$ -silyl acetates with ketones and aldehydes to give  $\alpha,\beta$ -unsaturated esters had been reported (ref. 22), this reaction had not been extended to  $\alpha$ -substituted- $\alpha$ -silyl esters. It was of interest to study this useful reaction with our  $\alpha$ -methyl-diphenylsilyl esters both from the standpoint of the sterically rather bulky methyl-diphenylsilyl group and the potential for incorporating  $\alpha$ -substitution into this transformation. It was pleasing to find that the reaction proceeds as hoped to give  $\alpha$ -substituted- $\alpha,\beta$ -unsaturated esters in good yields (ref. 23). (eq. 7) Unfortunately, the stereospecificity is not high being usually about 4:1 favoring the Z isomer. This reaction was extended to  $\alpha$ -(methyl-diphenylsilyl)- $\gamma$ -butyrolactones to give  $\alpha$ -ylidene- $\gamma$ -lactones (ref. 24). (eq. 8) This convenient methodology was applied towards an efficient, racemic synthesis of the marine natural product ancepsenolide (ref. 24). (eq. 9)

 **$\alpha$ -Silyl ketones and silyl enol ethers**

It was found that although the  $\alpha$ -methyl-diphenylsilyl esters would react with a Grignard reagent and then an organolithium reagent to give olefins, the reaction with an excess of a Grignard reagent leads to  $\alpha$ -methyl-diphenylsilyl ketones upon careful hydrolysis, with only small amounts of the olefin (ref. 25). (eq. 10) This general methodology has been applied to the synthesis of  $\alpha$ -methyl-diphenylsilyl ketones (ref. 26), selectively protected 1,4- and 1,5-diketones (refs. 27, 28), and to the synthesis of a component of the sex attractant for the Douglas Fir Tussock moth (ref. 26). (eq. 11) 4-Oxo acids and 1,4-diketones can be prepared by the reaction of a Grignard reagent with  $\alpha$ -(methyl-diphenylsilyl)- $\gamma$ -lactones when the resulting crude adduct is oxidized (ref. 29).



Scheme 1



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