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STOICHIOMETRIC GENERATION OF MAGNESIUM HOMOENOLATE EQUIVALENTS FROM ACYLTRIMETHYLSILANES. SYNTHESIS OF 1,6-DIKETONE DERIVATIVES

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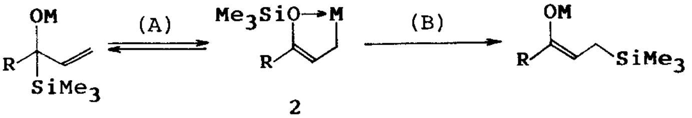
Summary: Treatment of various acyltrimethylsilanes with vinylmagnesium bromide has allowed a stoichiometric generation of the corresponding 3-(trimethylsiloxy)allylmagnesiums, which, in the presence of copper(I) trimethylsilylacetylide, undergo conjugate addition to several enones to afford the corresponding 1,6-diketone derivatives in good yields.

Although use of homoenolate anions is not so general as that of enolates in synthetic organic chemistry, their importance has been well recognized,[1] and several types of metal homoenolates and their equivalents have recently been described by us[2] and others.[3]

In connection with such synthetic purposes, we previously reported a unique behavior of 1-(trimethylsilyl)allylic alcohols **1** as homoenolate precursors.[4] On an equilibrium (A) with lithium homoenolates **2**, alkoxides of **1** are usually much favored due to greater electronegativity of oxygen, but an acceleration to move (A) to the homoenolate side has been induced on a basis of steric hindrance around silyl group.[5] However, the resulting **2** usually undergo an irreversible isomerization (B)[6] to the corresponding enolates of β-silyl ketones **3** under such conditions, which has made it incapable to effect a stoichiometric generation of **2** required for several synthetic elaborations such as conjugate addition reactions.

Various examinations have disclosed a remarkable effect of a metal cation on the isomerization (B) and use of magnesium alkoxides has brought about a great success for generation of **2** (M = MgBr). Thus, treatment of acyltrimethylsilanes **4**[7] with vinylmagnesium bromide in THF and a subsequent quenching

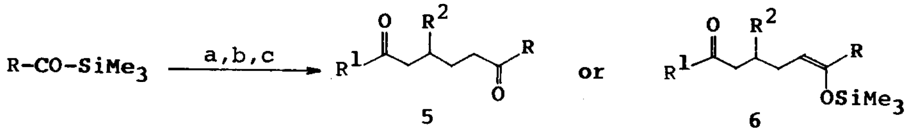


(Eq 1)

the reaction mixture gave the corresponding alcohols 1 and/or enol silyl ethers without any formation of **3**. Acylsilanes **4** bearing α-substituents larger than ethyl group afforded (Z)-isomers of enol silyl ethers exclusively.

Stoichiometric formation of magnesium homoenolates **2** has been confirmed by quenching the reaction mixture with deuterium oxide, giving the deuterated enol silyl ether over 90% yield in every case. These magnesium homoenolates react with ketones or acyl chlorides on their α-position predominantly or exclusively.

Several efforts have also been made to find optimum conditions for transfer of homoenolate moieties from magnesium to copper(I). Among various copper(I) salts, only Cu(I) trimethylsilylacetylide has proved to be very effective and the resulting organocopper species undergo the expected 1,4-



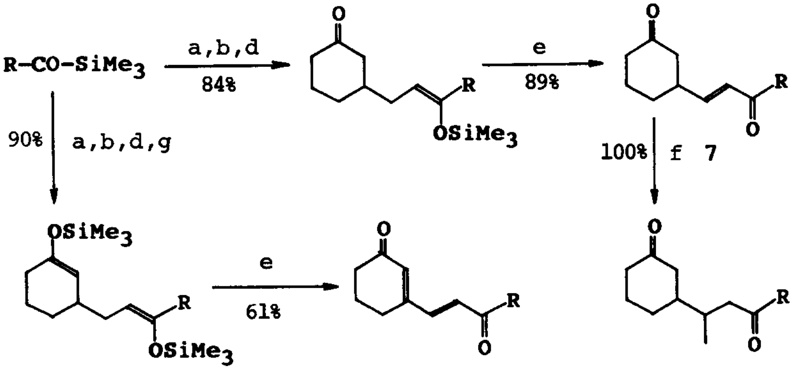
a) CH_2=CHMgBr. b) $Me_3SiC{\equiv}CCuSMe_2$. c) R^1-CO-CH=CHR^2 (Eq 2)

Table. Conjugate Addition Reactions of Copper Homoenolates.[a]

Enones	R of **2**	Yield(%) of **5**
Cyclohexenone	$(C_2H_5)_2CH$-	86
	$C_6H_5CH(C_2H_5)$-	(84)[b]
	$C_6H_5CH(i\text{-}C_3H_7)$-	88
3-Methylcyclohexenone	$C_6H_5CH(C_2H_5)$-	(74)
	$C_6H_5CH(i\text{-}C_3H_7)$-	78
2-Hexenal	$C_6H_5CH(C_2H_5)$-	(49)[c]
3-Hepten-2-one	$C_6H_5CH(C_2H_5)$-	(64, 96[c])
	$C_6H_5CH(i\text{-}C_3H_7)$-	65
Ethyl Acrylate	$C_6H_5CH(C_2H_5)$	(58)[d]
Ethyl 2-Hexenoate	$C_6H_5CH(C_2H_5)$-	(49)[e]

[a] Reactions were performed with equimolar amounts of enones and copper homoenolates, otherwise noted (see the text). [b] Numbers in parentheses represent the yield of **6**. [c] With 1.5 equiv of the copper homoenolate. [d] The reaction was carried out with 2 equiv of the homoenolate in ether for 6 h at -20 °C. [e] The reaction was performed for 9 h at 0 °C.

addition reaction to several enones to afford the corresponding 1,6-diketones **5** in good yield. Careful workup of the reaction mixture has allowed an isolation of the diketone as its mono-silyl ether **6**, which can be converted to the ene dione **7**. Although substituted vinyl Grignard reagents[8] are not employable for the present purposes, various alkyl groups can be introduced on the ene dione **7**, which has compensated a failure of generation of substituted homoenolates. Further, bis-silyl ethers can also be obtained in good yield by quenching the reaction mixture with a chlorosilane. Typical examples for synthetic applications are illustrated in Fig 1.

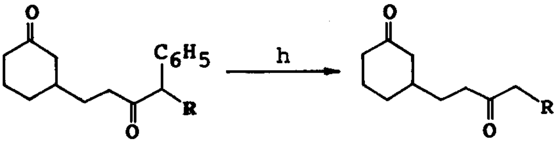


(Fig 1)

R = $C_6H_5CH(C_2H_5)$-

a) CH_2=CHMgBr. b) $Me_3SiC{\equiv}CCuSMe_2$. d) 2-cyclohexenone.
e) $Pd(OAc)_2$. f) $(CH_3)_2CuLi$. g) Me_3SiCl.

Although a range of application seems to be restricted to **2** bearing <u>sec</u>-alkyl groups, such limitation may be removed by using an appropriate α-phenylacylsilane. Application of an aromatic ring oxidation to the the resulting benzylic ketones afford the corresponding diketones in excellent yield through an initial formation of β-keto acids followed by their decarboxylation. Typical examples are shown in Eq 3. Thus, a combined use with this oxidative cleavage[9] has broaden the scope for introduction of several types of homoenolate moieties.



R = C_2H_5 85%
$CH(CH_3)_2$ 78%

(Eq 3)

h) $RuCl_3 3H_2O$ and $NaIO_4$

The following procedures are representative. 2-Phenylbutyryltrimethylsilane (0.1 mmol) was treated with vinylmagnesium bromide (0.1 mmol) in THF (0.5 ml) at room temperature for 10 min and the resulting solution was added to an ether (4 ml) solution of $Me_3SiC{\equiv}CCuSMe_2$ (0.12 mmol) at -20° C. Then, 2-cyclohexenone (0.1 mmol) was added and it was stirred for 1 hr at that temperature. After quenching the reaction mixture with $THF\text{-}H_2O$ (9:1) followed by extraction with hexane, removal of the solvnts gave the corresponding **6**, which on treating with $Pd(OAc)_2$,[10] afforded **7** in 76% yield.

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