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"ONE POT" DOUBLE CARBON-CARBON LINKAGES ON THE NEIGHBORING CARBONS VIA AN ENOL ETHER AS A REACTION INTERMEDIATE[1]

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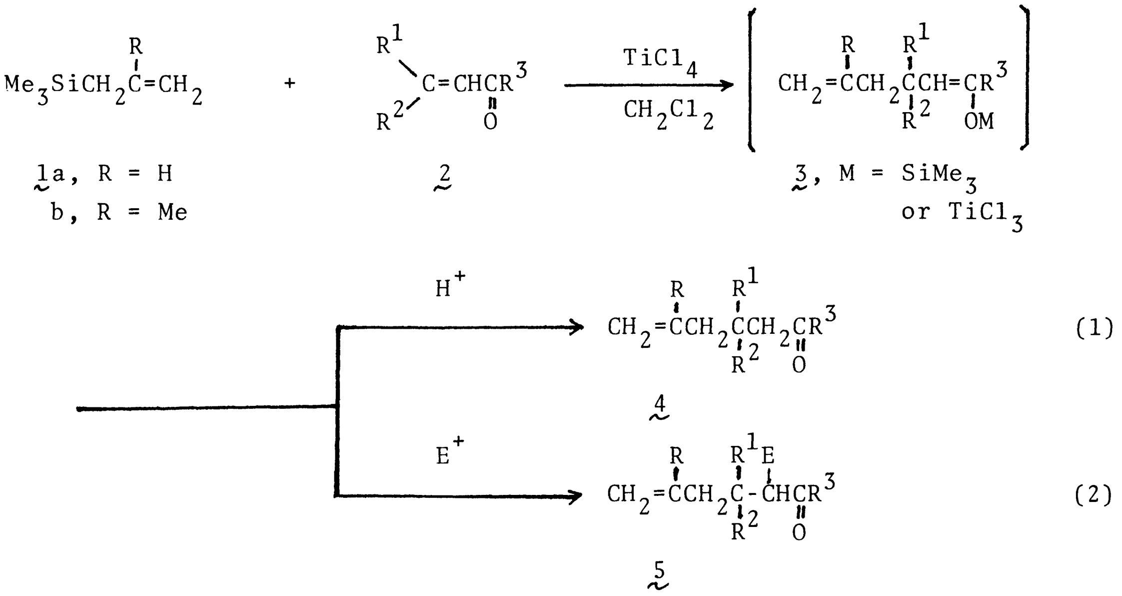
Two new "one pot" double alkylation reactions, 1) allylation of α,β-enones with allylsilanes and subsequent reaction with electrophiles, and 2) acylation of α-siloxyallylsilanes with acid halides followed by consecutive introduction of other electrophiles on the neighboring carbon atom, are reported.

Recently it has been reported from this laboratory that allylsilanes are highly effective reagents for allylation of a variety of electrophiles with regiospecific transposition in an allylic group of allylsilanes.[2,3] In conjugate addition of allylsilanes(**1**) to α,β-enones(**2**), an enolate(**3**) was considered as an intermediate, and actually δ,ε-enone(**4**) was obtained in good yield by protonation of the intermediate.[3d] Therefore, the reaction of the intermediates with carbon electrophiles was expected to result in the formation of products with an additional carbon-carbon bond (**5**), since the reaction of metal (silicon or titanium) enolates with electrophiles has been well documented.[4] Reactions in which two (or more) carbon-carbon linkages take place stepwise on the neighboring carbons, particularly, in one pot operation, are interesting and important to constructing the framework of organic molecules.[5]



1a, R = H
b, R = Me

2

3, M = SiMe$_3$ or TiCl$_3$

4

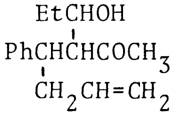
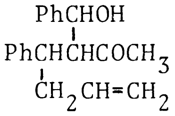
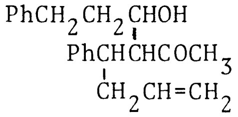
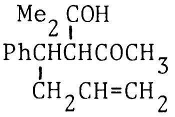
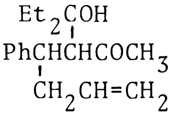
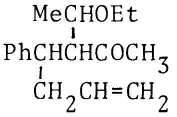
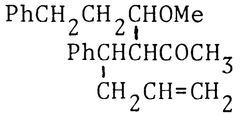
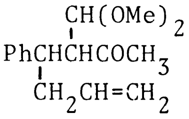
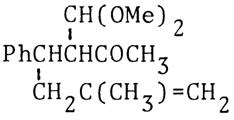
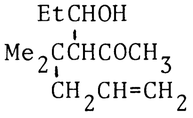
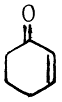
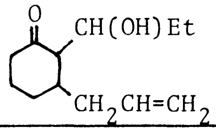
5

$$\mathrm{Me_3SiCH_2\overset{R}{C}{=}CH_2} + \mathrm{\underset{R^2}{\overset{R^1}{>}}C{=}CH\underset{O}{\overset{}{C}}R^3} \xrightarrow[\mathrm{CH_2Cl_2}]{\mathrm{TiCl_4}} \left[\mathrm{CH_2{=}\overset{R}{C}CH_2\underset{R^2}{\overset{R^1}{C}}CH{=}\underset{OM}{C}R^3}\right]$$

$$\xrightarrow{\mathrm{H^+}} \mathrm{CH_2{=}\overset{R}{C}CH_2\underset{R^2}{\overset{R^1}{C}}CH_2\underset{O}{C}R^3} \qquad (1)$$

$$\xrightarrow{\mathrm{E^+}} \mathrm{CH_2{=}\overset{R}{C}CH_2\underset{R^2}{\overset{R^1}{C}}\text{-}\overset{E}{C}H\underset{O}{C}R^3} \qquad (2)$$

Table.1. Consecutive reactions of allylsilanes **1** with α,β-enones followed by other electrophiles in the presence of $TiCl_4$ in CH_2Cl_2

Entry	Allylsilane	α,β-Enone	Electrophile	Conditions[a,b]	Product	(% yield)[c]
1	**1a**	PhCH=CHCOCH$_3$ **13**	EtCHO	-30°C, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{EtCHOH}{C}HCOCH_3}$	(64)
2	**1a**	**13**	PhCHO	-30°C, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{PhCHOH}{C}HCOCH_3}$	(51)
3	**1a**	**13**	PhCH$_2$CH$_2$CHO	-30°C, 2h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{PhCH_2CH_2CHOH}{C}HCOCH_3}$	(77)
4	**1a**	**13**	Me$_2$CO	rt, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{Me_2COH}{C}HCOCH_3}$	(56)
5	**1a**	**13**	Et$_2$CO	rt, 4h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{Et_2COH}{C}HCOCH_3}$	(19)
6	**1a**	**13**	MeCH(OEt)$_2$	-30°C, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{MeCHOEt}{C}HCOCH_3}$	(63)
7	**1a**	**13**	PhCH$_2$CH$_2$CH(OMe)$_2$	-30°C, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{PhCH_2CH_2CHOMe}{C}HCOCH_3}$	(43)
8	**1a**	**13**	CH(OMe)$_3$	-55°C, 1h	 $\mathrm{Ph\underset{CH_2CH=CH_2}{CH}\overset{CH(OMe)_2}{C}HCOCH_3}$	(72)
9	**1b**	**13**	CH(OMe)$_3$	-78°C, 3h[d]	 $\mathrm{Ph\underset{CH_2C(CH_3)=CH_2}{CH}\overset{CH(OMe)_2}{C}HCOCH_3}$	(62)
10	**1a**	Me$_2$C=CHCOCH$_3$	EtCHO	rt, 1h	 $\mathrm{Me_2\underset{CH_2CH=CH_2}{C}\overset{EtCHOH}{C}HCOCH_3}$	(20)
11	**1a**		EtCHO	-78°C, 1h		(50)

a. The reaction of **1a** with α,β-enones was carried out at -30°C for 10-30min unless otherwise noted. b. Conditions for the subsequent reaction with another electrophile. c. Yields after isolation by TLC. d. Condition at -78°C for 2min was used for the first step.

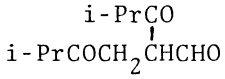
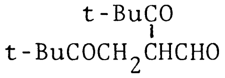
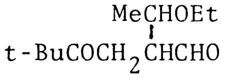
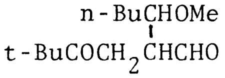
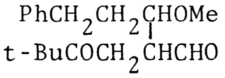
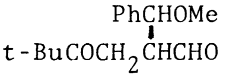
The expectation became reality when we have found that carbon electrophiles such as aldehydes, ketones, and acetals can react with the intermediate enolate 3 to form a new carbon-carbon bond on the α-carbon after the allylation at the β-carbon of α,β-enones in one pot operation. The results are listed in Table 1.[6]

Aldehydes afford satisfactory results rather than ketones presumably due to the less steric hindrance around the carbonyl group. It is worthwhile to note that methyl orthoformate is one of the most reactive electrophiles. On the contrary, no satisfactory result was obtained with alkyl halides,[7] alkyl tosylates, and acid halides. Titanium tetrachloride, among various Lewis acids, is the most effective activator over two stages of the reaction.

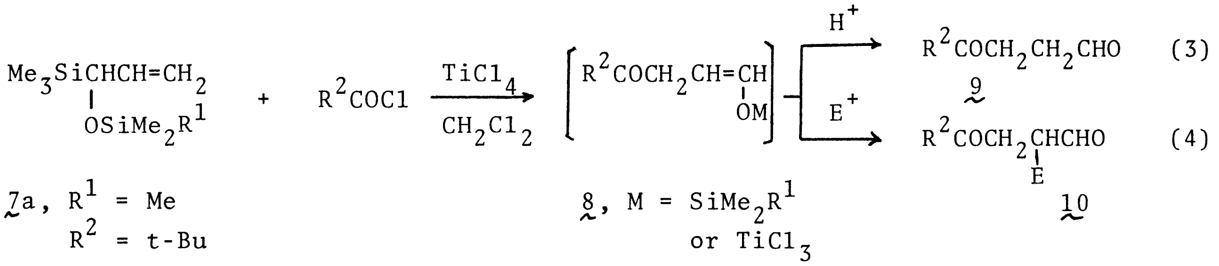
As a general procedure, to a solution of an α,β-enone(1.0 mmol) and titanium tetrachloride(1.0 mmol) in dry dichloromethane(3 ml) at -78°C, an allylsilane (1.1 mmol) in dichloromethane(3 ml) was added with stirring under nitrogen. After stirring under a given condition, another electrophile(1.1 mmol) was added and the mixture was further stirred under a given condition and hydrolyzed. After usual workup, a product was isolated by the preparative tlc.

Acylation of α-siloxyallylsilanes with acid chlorides promoted by titanium tetrachloride can also produce an enolate(8) as an intermediate.[3g] Accordingly, instead of proton, other electrophiles can be used in the subsequent reaction. Indeed it was

Table 2. Reactions of α-siloxyallylsilanes(7) with acid halides followed by other electrophiles in the presence of TiCl_4 in CH_2Cl_2

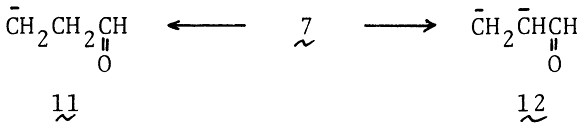
Entry	7	Acid Halide	Electrophile	Conditions[a]	Product	(% yield)[b]
1[c]	7b	i-PrCOCl	i-PrCOCl	-78°C 5.5h	 $\text{i-PrCOCH}_2\overset{\text{i-PrCO}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(54)
2[c]	7b	t-BuCOCl	t-BuCOCl	-78°C 5h	 $\text{t-BuCOCH}_2\overset{\text{t-BuCO}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(59)
3	7a	t-BuCOCl	MeCH(OEt)_2	-78°C ~ -30°C[d] 5h	 $\text{t-BuCOCH}_2\overset{\text{MeCHOEt}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(53)
4	7a	t-BuCOCl	n-BuCH(OMe)_2	-78°C ~ -20°C[d] 2h	 $\text{t-BuCOCH}_2\overset{\text{n-BuCHOMe}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(59)
5	7a	t-BuCOCl	$\text{PhCH}_2\text{CH}_2\text{CH(OMe)}_2$	-78°C ~ -25°C[d] 3.5h	 $\text{t-BuCOCH}_2\overset{\text{PhCH}_2\text{CH}_2\text{CHOMe}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(63)
6	7a	t-BuCOCl	PhCH(OMe)_2	-78°C ~ -20°C[d] 3hr	 $\text{t-BuCOCH}_2\overset{\text{PhCHOMe}}{\overset{\vert}{\text{C}}}\text{HCHO}$	(55)

a. Conditions for the second step. b. Yields after isolation by TLC. c. Two equivalents of the acid chloride were used. d. The reaction of 7a with pivaloyl chloride was carried out at -78°C for 3h.



$$\underset{\underset{R^2 = \text{t-Bu}}{\mathbf{7a},\ R^1 = \text{Me}}}{\underset{\mathrm{OSiMe_2R^1}}{\mathrm{Me_3SiCHCH{=}CH_2}}} + R^2COCl \xrightarrow[CH_2Cl_2]{TiCl_4} \underset{\mathbf{8},\ M = \mathrm{SiMe_2R^1}\ \text{or}\ \mathrm{TiCl_3}}{\left[R^2COCH_2CH{=}\underset{OM}{CH} \right]} \begin{cases} \xrightarrow{H^+} \underset{\mathbf{9}}{R^2COCH_2CH_2CHO} & (3) \\ \xrightarrow{E^+} \underset{\mathbf{10}}{R^2COCH_2\underset{E}{C}HCHO} & (4) \end{cases}$$

found that acyl halides or acetals were reactive for the present "one pot" reaction. The results are listed in Table 2.[6] Therefore, α-siloxyallylsilanes(7) can be viewed not only as the "homoenolate anion(11)" but also as the "dianion(12)" equivalents.



$$\underset{\mathbf{11}}{\bar{C}H_2CH_2\underset{O}{\overset{\|}{C}}H} \longleftarrow \mathbf{7} \longrightarrow \underset{\mathbf{12}}{\bar{C}H_2\bar{C}H\underset{O}{\overset{\|}{C}}H}$$

Acknoledgement: We thank Toshiba Silicone Co., Ltd., for a gift of chlorosilanes.

References and Notes

1. Chemistry of organosilicon compounds 124.
2. a) A. Hosomi and H. Sakurai, Tetrahedron Lett., 1295(1976); b) idem, ibid., 4041 (1977); c) idem, ibid., 2589(1978); d) A. Hosomi and H. Sakurai, J. Am. Chem. Soc., **99**, 1673(1977); e) A. Hosomi, M. Endo, and H. Sakurai, Chem. Lett., 941(1976); f) idem, ibid., 499(1978); g) A. Hosomi, H. Hashimoto, and H. Sakurai, J. Org. Chem., **43**, 2551(1978); h) A. Hosomi, A. Shirahata, and H. Sakurai, Tetrahedron Lett., 3043(1978); i) idem, Chem. Lett., 901(1978).
3. For other examples, see references cited in ref. 3d.
4. inter alia, a) T. Mukaiyama, K. Banno, and K. Narasaka, J. Am. Chem. Soc., **96**, 7504(1974); b) T. Mukaiyama and M. Hayashi, Chem. Lett., 15(1974); c) T. Mukaiyama and A. Ishida, ibid., 319(1975).
5. Indeed synthesis of sesquiterpenes,[a] prostaglandins,[b] and methyl jasmonate[c] are recently prepared by the double alkylation method using organocopper lithium. See, a) R. M. Coates and L. O. Sandefur, J. Org. Chem., **39**, 275(1974); b) R. A. Kretchmer and W. M. Schafer, ibid., **38**, 95(1973); G. H. Posner, J. J. Sterling, C. E. Whitten, C. M. Lentz, and D. J. Brundle, J. Am. Chem. Soc., **87**, 107(1975); G. H. Posner and C. M. Lentz, Tetrahedron Lett., 3215(1977); c) A. E. Greene and P. Crabbe, ibid., 4867(1976).
6. Satisfactory ir and nmr spectra, and elemental analysis were obtained for all products.
7. t-Butyl chloride is effective for the t-butylation of silyl enol ethers under the similar condition. See, a) T. H. Chan, I. Paterson, and J. Pinsonault, Tetrahedron Lett., 4183(1977); b) M. T. Reetz and W. F. Mainer, Angew. Chem. Int. Ed. Engl., **17**, 48(1978).

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