Mechanism of Mukaiyama−Michael Reaction of Ketene Silyl Acetal: Electron Transfer or Nucleophilic Addition?

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Received July 18, 1995⊗

Mechanism of Mukaiyama-Michael reaction of ketene silyl acetal has been discussed. The competition reaction employing various types of ketene silyl acetals reveals that those bearing more substituents at the β-position react preferentially over less substituted ones. However, when ketene silyl acetals involve bulky siloxy and/or alkoxy group(s), less substituted compounds react preferentially. The Lewis acids play an important role in these reactions. Enhanced preference for the more sterically demanding Michael adducts is obtained with $Bu_2Sn(OTf)_2$, $SnCl_4$, and Et_3SiClO_4 in the former reaction while $TiCl_4$ gives the highest selectivity for the less sterically demanding products in the latter case. These results are interpreted in terms of alternative reaction mechanisms. The reaction of less bulky ketene silyl acetals are initiated by electron transfer from these compounds to a Lewis acid. On the other hand, bulkier ketene silyl acetals undergo a ubiquitous nucleophilic reaction. Such a mechanistic change is discussed based on a variety of experimental results as well as the semiempirical PM3 MO calculations.

The Mukaiyama version of the Michael reaction of ketene silyl acetals is recognized as an important reaction in modern synthetic chemistry.[1] Of particular significance is the role of Lewis acids that can complement an alternative alkali metal enolate method. The Lewis acids are generally believed to activate carbonyl substrates through coordination for nucleophilic attack of ketene silyl acetals. In some cases, however, Lewis acids have been reported to act as an electron acceptor from ketene silyl acetals.[2] In this context, we have recently reported that β-methyl-substitution of ketene silyl acetals increases the electron density rendering the donor more susceptible to the electron transfer oxidation,[3] although it also generally increases the steric hindrance of the reaction center, thereby reducing the reactivity of the nucleophilic attack toward electrophiles.[4] Operation of these two opposing effects leads to the possibility of a mechanistic change from ubiquitous nucleophilic processes to novel electron transfer pathways. The electron transfer vs nucleophilic process dichotomy is one of the central propositions in the reaction mechanism,[5] and thus parallel assessment of both processes would be valuable. Although discussion of the nucleophilic mechanism has so far been advanced mostly on the basis of the product stereochemistry, it is desirable to gain insight about the transition state on the basis of the reactivities.

We report herein for the first time the extensive comparison of the reactivities of various ketene silyl acetals in the Mukaiyama−Michael reaction.[6] The relative reactivities of ketene silyl acetals have been found to vary depending on the β-methyl-substitution and silyl groups of ketene silyl acetals, substrates, and also Lewis acids. Such change in the reactivity of ketene silyl acetals particularly with β-methyl-substitution may provide valuable insight into the electron transfer vs nucleophilic process dichotomy.

Results

Competition Reaction. The relative reactivities of ketene silyl acetals toward α-enone in the presence of Lewis acid were determined from competition experiments. When two different ketene silyl acetals A and B react with the same α-enone in the presence of a Lewis acid, the ratio of reaction rate, $\{-d[A]/dt\}/\{-d[B]/dt\} = d[A]/d[B]$ may be given by eq 1,

$$d[A]/d[B] = (k_A/k_B)[A]/[B] \quad (1)$$

where k_A and k_B are the rate constants for ketene silyl acetals A and B, and [A] and [B] are the concentrations, respectively. From eq 1 is derived eq 2, where $[A]_0$ and $[B]_0$ are the initial concentration of A and B, respectively.

$$\ln([A]/[A]_0)/\ln([B]/[B]_0) = k_A/k_B \quad (2)$$

Since the product yields Y_A (%) and Y_B (%) derived from A and B are given by $Y_A/100 = 1 - [A]/[A]_0$ and $Y_B/100 = 1 - [B]/[B]_0$, respectively, from eq 2 is derived the ratio of the reactivity of two different ketene silyl acetals ($r = k_A/k_B$) as given by eq 3.[7]

$$r = k_A/k_B = \ln(1 - Y_A/100)/\ln(1 - Y_B/100) \quad (3)$$

The reactivity ratios (r) of all combinations of β,β-disubstituted ketene silyl acetals (**2a**−**c**), monosubsti-

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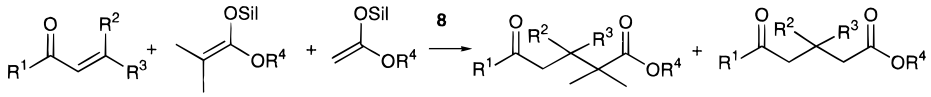
⊗ Abstract published in *Advance ACS Abstracts,* March 15, 1996.

(1) Oare, D. A.; Heathcock, C. H. In *Topics in Stereochemistry*; Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1991; Vol. 20, p 87.
(2) (a) Reetz, M. T.; Schwellnus, K.; Hübner, F.; Massa, W.; Schmidt, R. E. *Chem. Ber.* **1983**, *116*, 3708. (b) Totten, G. E.; Wenke, G.; Rhodes, Y. E. *Synth. Commun.* **1985**, *15*, 291. (c) Ali, S. M.; Rousseau, G. *Tetrahedron* **1990**, *46*, 7011. (d) Quendo, A.; Ali, S. M. Rousseau, G. *J. Org. Chem.* **1992**, *57*, 6890. (e) Odenkirk, W.; Whelan, J.; Bosnich, B. *Tetrahedron Lett.* **1992**, *33*, 5729.
(3) Fukuzumi, S.; Fujita, M.; Otera, J.; Fujita, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10271.
(4) Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938.
(5) Pross, A.; Shaik, S. S. *Acc. Chem. Res.* **1983**, *16*, 363. Pross, A. *Acc. Chem. Res.* **1985**, *18*, 212. Shaik, S. S. *Prog. Phys. Org. Chem.* **1985**, *15*, 197. Pradhan, S. K. *Tetrahedron* **1986**, *42*, 6351. Kochi, J. K. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1227. Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414. Savéant, J.-M. *Adv. Phys. Org. Chem.* **1990**, *26*, 1. Shaik, S. S. *Acta Chem. Scand.* **1990**, *44*, 205. Fukuzumi, S. In *Advances in Electron Transfer Chemistry*; Mariano, P. S., Ed.; JAI Press: Greenwich, 1992; Vol. 2, p 65. Mattalia, J.-M.; Vacher, B.; Samat, A.; Chanon, M. *J. Am. Chem. Soc.* **1992**, *114*, 4111 and references cited therein.

S0022-3263(95)01296-5 CCC: $12.00

Table 1. Competition between *β,β*-Disubstituted and Unsubstituted Ketene Silyl Acetals

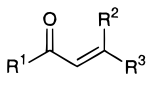


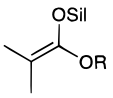
1 **2** **4** **5** **7**

entry	1	2	4	8	yield, % 5	yield, % 7	5:7	R^1	R^4	*r*	(r_{pr})
1	**1a** (R^2, R^3 = Me)	**2a**	**4a**	**8a**	**5a**, 85	**7a**, 0	100:0	Ph	Et	100:0	(100:0)
2				**8b**	95	0	100:0	Ph	Et	100:0	(100:0)
3				**8c**	93	0	100:0	Ph	Et	100:0	(100:0)
4				**8d**	97	3	97:3	Ph	Et	99:1	(90:10)
5	**1b** (R^2, R^3 = Me)	**2a**	**4a**	**8b**	**5b**, 21	**7b**, 0	100:0	^{t}Bu	Et	100:0	(100:0)
6				**8c**	53	4	93:7	^{t}Bu	Et	95:5	(97:3)
7				**8d**	62	25	(71:29)	^{t}Bu	Et	77:23	(85:15)
8	**1c** (R^2 = H, R^3 = Me)	**2a**	**4a**	**8b**	**5c**, 45	**7c**, 0	100:0	^{t}Bu	Et	100:0	(100:0)
9		**2b**	**4b**	**8b**	**5d**, 3	**7d**, 34	9:91	^{t}Bu	Me[a]	7:93	(1:99)
10				**8c**	3	38	7:93	^{t}Bu	Me[a]	6:94	(1:99)
11				**8d**	4	72	5:95	^{t}Bu	Me[a]	3:97	(4:96)
12		**2c**	**4c**	**8c**	**5e**, 4	**7e**, 50	6:94	^{t}Bu	Bor	6:94	(20:80)
13				**8d**	0	69	0:100	^{t}Bu	Bor	0:100	(5:95)

[a] Determined as the methyl ester: see Experimental Section.

tuted (**3a**−**c**), and unsubstituted (**4a**−**c**) counterparts





1a R^1 = Ph R^2 = Me R^3 = Me **2a** Sil = TES R = Et

b = ^{t}Bu = Me = Me **b** = TBS = ^{t}Bu

c = ^{t}Bu = H = Me **c** = TBS = Bor

d = Ph = H = Me **d** = TMS = Me

e = Ph R^2, R^3 = Me, Et **e** = TBS = Et

3a Sil = TES R = Et **4a** Sil = TES R = Et

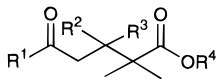
b = TBS = ^{t}Bu **b** = TBS = ^{t}Bu

c = TBS = Bor **c** = TBS = Bor

d = TMS = Me **d** = TBS = Et

e = TBS = Et

toward α-enones (**1a**−**c**) were fully examined in the presence of various Lewis acids: $Bu_2Sn(OTf)_2$ (**8a**); $SnCl_4$ (**8b**); Et_3SiClO_4 ($TESClO_4$) (**8c**); $TiCl_4$ (**8d**). The results of competition between **2a**−**c** and **4a**−**c**, **2a**−**c** and **3a**−**c**, and **3a**−**c** and **4a**−**c** are shown in Tables 1−3. The competition between *β,β*-disubstituted ketene silyl acetal **2a** and the unsubstituted counterpart **4a** toward α-enone **1a** results in preferential formation of more hindered adduct **5a** over **7a** (Table 1, entries 1−4). The preference is remarkable as shown by the >99:1 reactivity ratio, $r_{2/4}$, in the cases of Lewis acids **8a**−**c** (the sum of ratio is taken as 100).[8] It should be noted, however, that **8d** gave rise to lower selectivity (97:3). Such remarkably enhanced



5a R^1 = Ph R^2 = Me R^3 = Me R^4 = Et

b = ^{t}Bu = Me = Me = Et

c = ^{t}Bu = H = Me = Et

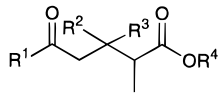
d = ^{t}Bu = H = Me = Me

e = ^{t}Bu = H = Me = Bor

f = Ph = H = Me = Et

g = Ph = Me = Me = Me

h = Ph = Me = Et =Et



6a R^1 = Ph R^2 = Me R^3 = Me R^4 = Et

b = ^{t}Bu = Me = Me = Et

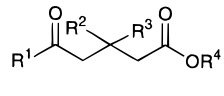
c = ^{t}Bu = H = Me =Et

d = ^{t}Bu = H = Me = Me

e = ^{t}Bu = H = Me = Bor

f = Ph = H = Me = Me

g = Ph = Me = Et = Et



7a R^1 = Ph R^2 = Me R^3 = Me R^4 = Et

b = ^{t}Bu = Me = Me = Et

c = ^{t}Bu = H = Me = Et

d = ^{t}Bu = H = Me = Me

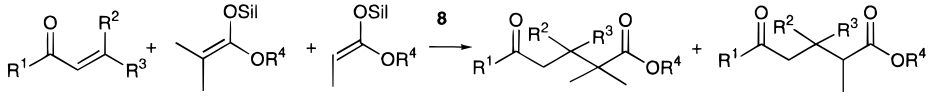
e = ^{t}Bu = H = Me = Bor

reactivity by *β*-substitution with methyl group is also observed for the competition between **2a** and monosub-

(6) For a preliminary communication: Sato, T.; Wakahara, Y.; Otera, J.; Nozaki, H.; Fukuzumi, S. *J. Am. Chem. Soc.* **1991**, *113*, 4028.

(7) Although eq 3 can be reduced to a simple relation, $k_A/k_B = Y_A/Y_B$, under the experimental conditions such that the concentrations of A and B are much greater than that of α-enone, the competition experiments were performed under the normal conditions for the synthetic purpose in order to avoid the use of extremely high concentrations of A and B (≫1 M).

Table 2. Competition between *β,β*-Disubstituted and *β*-Monosubstituted Ketene Silyl Acetals

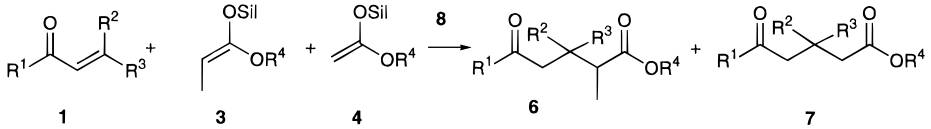


1 **2** **3** **5** **6**

					yield, %					
entry	**1**	**2**	**3**	**8**	**5**	**6**	**5:6**	R^1	R^4	*r*
1	**1a** (R^2, R^3 = Me)	**2a**	**3a**	**8a**	**5a**, 84	**6a**, 0	100:0	Ph	Et	100:0
2				**8b**	89	8	92:8	Ph	Et	96:4
3				**8c**	88	12	88:12	Ph	Et	94:6
4				**8d**	65	28	70:30	Ph	Et	76:24
5	**1b** (R^2, R^3 = Me)	**2a**	**3a**	**8b**	**5b**, 22	**6b**, 2	85:15	^{t}Bu	Et	92:8
6				**8c**	53	27	67:33	^{t}Bu	Et	71:29
7				**8d**	55	32	63:27	^{t}Bu	Et	67:33
8	**1c** (R^2 = H, R^3 = Me)	**2a**	**3a**	**8b**	**5c**, 60	**6c**, 6	91:9	^{t}Bu	Et	94:6
9		**2b**	**3b**	**8b**	**5d**, 14	**6d**, 86	14:86	^{t}Bu	Me[a]	3:93
10				**8c**	4	55	7:93	^{t}Bu	Me[a]	5:95
11				**8d**	1	86	1:99	^{t}Bu	Me[a]	1:99
12		**2c**	**3c**	**8c**	**5e**, 25	**6e**, 36	41:59	^{t}Bu	Bor	39:61
13				**8d**	29	74	28:72	^{t}Bu	Bor	20:80

[a] Determined as the methyl ester; see Experimental Section.

Table 3. Competition between *β*-Monosubstituted and Unsubstituted Ketene Silyl Acetals



1 **3** **4** **6** **7**

					yield, %					
entry	**1**	**3**	**4**	**8**	**6**	**7**	**6:7**	R^1	R^4	*r*
1	**1a** (R^2, R^3 = Me)	**3a**	**4a**	**8a**	**6a**, 67	**7a**, 0	100:0	Ph	Et	100:0
2				**8b**	69	0	100:0	Ph	Et	100:0
3				**8c**	78	13	86:14	Ph	Et	92:8
4				**8d**	59	26	69:31	Ph	Et	75:25
5	**1b** (R^2, R^3 = Me)	**3a**	**4a**	**8b**	**6b**, 12	**7b**, 0	100:0	^{t}Bu	Et	100:0
6				**8c**	43	5	90:10	^{t}Bu	Et	92:8
7				**8d**	51	23	69:31	^{t}Bu	Et	73:27
8	**1c** (R^2 = H, R^3 = Me)	**3a**	**4a**	**8b**	**6c**, 28	**7c**, 1	97:3	^{t}Bu	Et	97:3
9		**3b**	**4b**	**8b**	**6d**, 3	**7d**, 43	6:94	^{t}Bu	Me[a]	5:95
10				**8c**	3	36	7:93	^{t}Bu	Me[a]	6:94
11				**8d**	38	47	45:55	^{t}Bu	Me[a]	43:57
12		**3c**	**4c**	**8c**	**6e**, 22	**7e**, 48	31:69	^{t}Ru	Bor	28:72
13				**8d**	14	59	19:81	^{t}Bu	Bor	16:84

[a] Determined as the methyl ester: see Experimental Section.

stituted compound **3a** and also between **3a** and the unsubstituted counterpart **4a** as shown in Tables 2 and 3, respectively. The same trend also holds with α-enones **1b** and **1c** (entries 5−8, Table 1−3). Since the reactivity ratio of **2a**−**c** vs **4a**−**c** in Table 1 can be derived from that of **2a**−**c** vs **3a**−**c** together with that of **3a**−**c** vs **4a**−**c**, the consistency of data is checked by comparing the $r_{2/4}$ values in Table 1 with the products ($r_{pr} = r_{2/3} \times r_{3/4}$) of the corresponding *r* values in Table 2 ($r_{2/3}$) and 3 ($r_{3/4}$), respectively. The r_{pr} values as listed in Table 1 agree qualitatively with the experimental values determined directly, demonstrating the validity of the reactivity ratios.

Noticeably, a dramatic change was seen when a series of *tert*-butyldimethylsilyl (TBS) enolates of *tert*-butyl esters (**2b**, **3b**, and **4b**) were employed (entries 9−11 in Table 1−3). These ketene silyl acetals sluggishly reacted with *β,β*-disubstituted enones but with *β*-monosubstituted one **1c** in reasonable yields. Among the Lewis acids, $TiCl_4$ induced the highest selectivities except in the case of the entry 11 in Table 3 in sharp contrast to the reaction with the aforementioned less sterically demanding ketene silyl acetals (**2a**, **3a**, **4a**). These normal selectivities in terms of the conventional nucleophilic mechanism can be attributed to incorporation of large TBS and *tert*-butyl groups. Thus, ketene silyl acetals (**2c**, **3c**, and **4c**) which were derived from bornyl esters exhibited similar tendencies (entries 12, 13 in Table 1−3).

The normal selectivity was attained even with less bulky ketene silyl acetals under certain other conditions. For example, the ether−$LiClO_4$ system which had been found to effect the Michael reaction of ketene silyl acetals by Grieco et al.[9,10] afforded predominantly the less hindered products in the competition reactions (Scheme 1).[11] Et_2AlCl is another Lewis acid which gave rise to the same outcome (Scheme 2). Further noteworthy is the reaction of *O,S*-ketene silyl acetals: even the trivial Lewis acids such as $SnCl_4$, $TESClO_4$, and $TiCl_4$ exhibited the normal selectivity (Table 4).

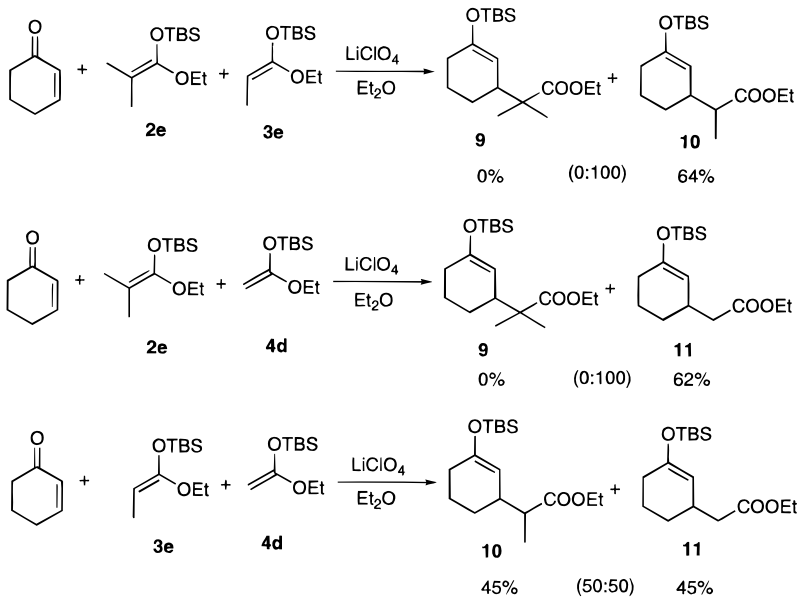
Influence of Lewis Acid. It is apparent from the above results that the Lewis acids have a profound

(8) The ratio of 100:0 includes the experimental error probably within ±2%. Thus, the ratio does not mean the infinite value. This means that the rate constant of **2** is at least two orders of magnitude greater than that of **4**.

(9) Grieco, P. A.; Cooke, R. J.; Henry, K. J.; VanderRoest, J. M. *Tetrahedron Lett.* **1991**, *32*, 4665.

(10) Reetz et al. has revealed the CH_2Cl_2−$LiClO_4$ system to be more powerful to trigger the Michael reaction: Reetz, M. T.; Fox, D. N. A. *Tetrahedron Lett.* **1993**, *34*, 1119.

Scheme 1



Scheme 2

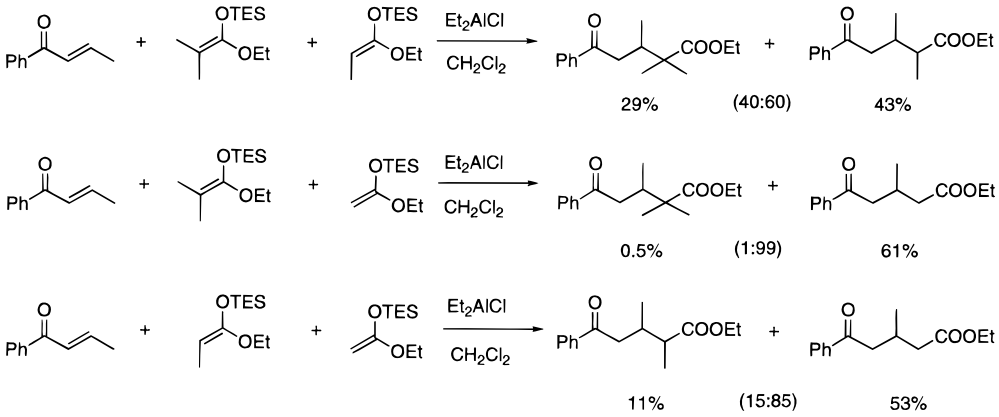
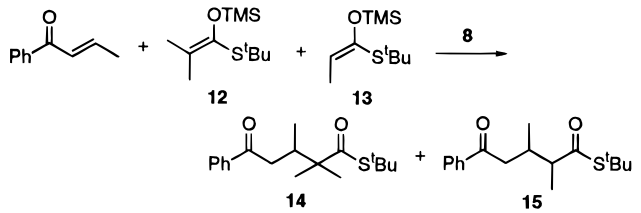
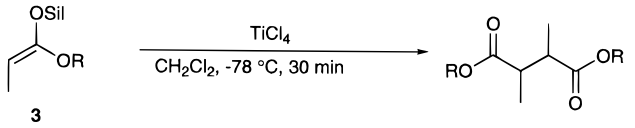


Table 4. Competition between *β,β*-Disubstituted and *β*-Monosubstituted *O,S*-Ketene Silyl Acetals



	yield, %		
8	**14**	**15**	**14:15**
8b	5	82	6:94
8c	1	96	1:99
8d	0	98	0:100

Table 5. $TiCl_4$-Promoted Coupling of Ketene Silyl Acetal



3	Sil	R	yield, %
3a	TES	Et	41
3b	TBS	^{t}Bu	63 (18)[a]
3c	TBS	Bor	52 (48)[a]

[a] The recovery of the propionate ester is given in the parentheses.

influence on the selectivity. Therefore, it is important to disclose the difference between the Lewis acids. Ojima et al.[12] and Rhodes et al.[2b] reported that ketene silyl acetals were converted to succinates upon treatment with $TiCl_4$ at room temperature. As Table 5 shows, the same reaction occurs even at −78 °C, the temperature at which our Michael reactions were carried out. In some cases, parent esters were detected simultaneously. The reaction with $SnCl_4$, on the other hand, proceeded differently. A CH_2Cl_2 solution of $SnCl_4$ and ketene silyl acetals (1:1 molar ratio) was stirred at −78 °C for 30 min. Addition of ether to this solution caused no precipitation indicative of absence of free $SnCl_4$.[13] The solution was warmed and volatile materials were evaporated in vacuo. NMR spectra of the residue in CD_2Cl_2 unambiguously confirmed α-stannyl esters to be produced quantitatively as shown in Table 6.[14]

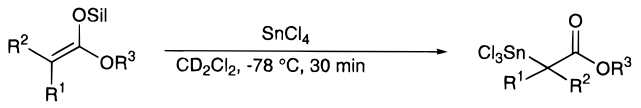
(11) Use of acyclic α-enones resulted in poor yields under the same reaction conditions.

(12) (a) Inaba, S.-I.; Ojima, I. *Tetrahedron Lett.* **1977**, 2009. (b) Hirai, K.; Ojima, I. *Tetrahedron Lett.* **1983**, *24*, 785.

(13) It was confirmed that, if $SnCl_4$ was present, an exothermic reaction immediately occurred to give precipitates of the $SnCl_4$−ether complex.

(14) Preparation of α-stannyl ketones from enol silyl ethers by an analogous transmetalation was reported: Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1983**, *24*, 3347.

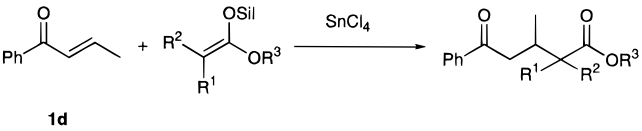
Table 6. Formation of α-Stannyl Esters



	ketene silyl acetal	yield, %[a]
2a	(R^1, R^2 = Me, R^3 = Et, Sil = TES)	81
2b	(R^1, R^2 = Me, R^3 = ^{t}Bu, Sil = TBS)	89
2d	(R^1, R^2, R^3 = Me, Sil = TMS)	100
3a	(R^1 = Me, R^2 = H, R^3 = Et, Sil = TES)	96
3b	(R^1 = Me, R^2 = H, R^3 = ^{t}Bu, Sil = TBS)	96
3d	(R^1, R^3 = Me, R^2 = H, Sil = TMS)	94

[a] Determined by ^{1}H NMR.

Table 7. Effect of the Amount of $SnCl_4$



1d

	ketene silyl acetal	equiv amount of $SnCl_4$	yield, %
3d	(R^1, R^3 = Me, R^2 = H, Sil = TMS)	1.0	**6f**, 6
		0.1	68
2a	(R^1, R^2 = Me, R^3 = Et, Sil = TES)	1.0	**5f**, 20
		0.2	70
		0.1	67
		0.05	80

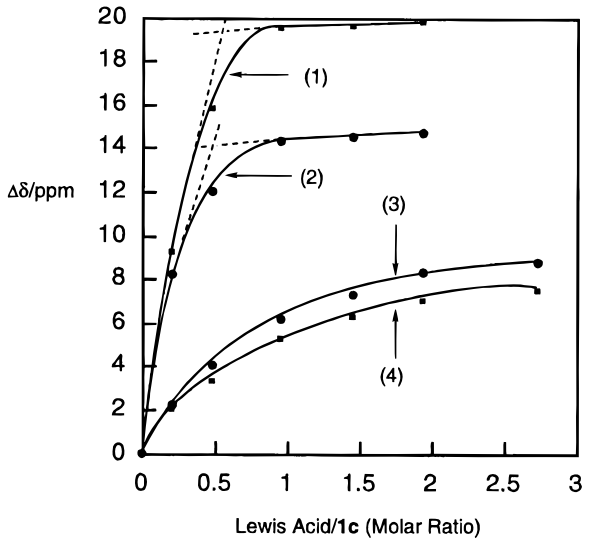
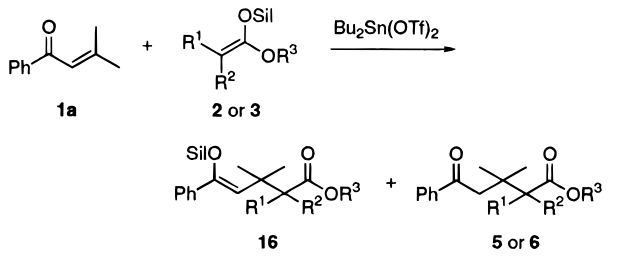


Figure 1. Dependence of ^{13}C chemical shifts of the C_3 and C_5 signals of 2,2-dimethyl-4-hexen-3-one (**1c**) upon the dosage of Lewis acids. (1) C_5 upon $TiCl_4$, (2) C_3 upon $TiCl_4$, (3) C_3 upon $SnCl_4$, and (4) C_5 upon $SnCl_4$.

In connection with the above findings, a rather unexpected effect of the $SnCl_4$ catalyst was found: the greater the amount of $SnCl_4$ catalyst used, the lower the yield of the Michael adduct. Reaction of **3d** with **1d** in the presence of a stoichiometric amount of $SnCl_4$ afforded only a 6% yield of the Michael adduct while a 68% yield was obtained with 0.1 equiv of $SnCl_4$ (Table 7). Similar results are given for **2a**.

Such variations of the reactivity with $SnCl_4$ and $TiCl_4$ may be partly associated with the different coordinating ability toward enone, which was confirmed by ^{13}C NMR spectroscopy. Figure 1 illustrates the change of the chemical shifts of the C_3 and C_5 signals of 2,2-dimethyl-4-hexen-3-one (**1c**) upon increasing the amount of added Lewis acids. Obviously, $TiCl_4$ causes more substantial low-field shift than $SnCl_4$ and formation of a 1:2 $TiCl_4$−**1c** complex is evident.

Table 8. Isolation of Silyl Enol Ether Intermediates

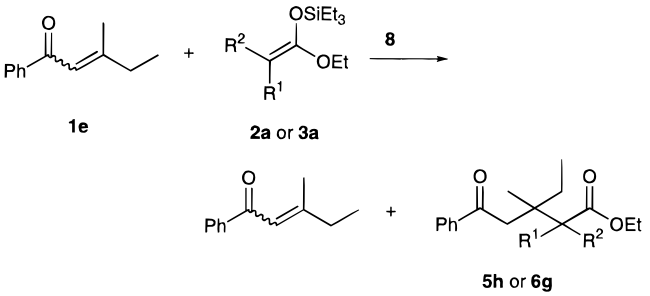


1a **2 or 3** **16** **5 or 6**

		yield, %[b]	
2 or 3	conditions[a]	**16**	**5 or 6**
2a	A	**16a**, 56	**5a**, 38
	B	69	<1
2d	A	**16b**, 77	**5g**, 6
	B	64	0
3a	A	**16c**, 58	**6a**, 42
	B	55	20

[a] A: Et_3N/hexane quench; B: in CH_2Cl_2/THF. [b] Isolated yield.

Table 9. Isomerization of *β,β*-Disubstituted α-Enone during Michael Addition



1e **2a or 3a** **5h or 6g**

1e	ketene silyl acetal	**8**	conversion, %	E:Z of recovred **1e**	diastereomer ratio of **6g**
E:*Z* = 99:1	**2a** (R^1, R^2 = Me)	**8a**	44	90:10	
		8b	74	92:8	
		8c	84	88:12	
E:*Z* = 1:99		**8a**	49	22:78	
		8b	61	22:78	
		8c	88	23:77	
E:*Z* = 99:1	**3a** (R^1 = Me; R^2 = H)	**8a**	79	90:10	56:44
		8b	68	88:12	55:45
E:*Z* = 1:99		**8a**	64	12:88	45:55
		8b	68	33:67	42:58
		8c	52	13:87	44:55

Enol silyl ethers of the Michael adducts **16** were obtained by quenching the $Bu_2Sn(OTf)_2$-catalyzed reaction with Et_3N (Table 8). Moreover, when the reaction was conducted in CH_2Cl_2−THF (9:1), the silyl ethers are feasible even after aqueous workup.

Isomerization of α-Enone. To gain further information about the reaction mechanism we prepared an unsymmetrically disubstituted α-enone **1e** and investigated the stereochemical isomerization during the Michael reaction (Table 9). Exposure of Lewis acids (1.0 equiv) such as **8a**, **8b**, or **8c** to **1e** in CH_2Cl_2 at −78 °C induced no isomerization of the enone. $TiCl_4$, however, resulted in the isomerization probably due to the HCl concomitant and, hence, was not used for the present purpose. Reaction of **1e** with ketene silyl acetals in the presence of the above Lewis acids was quenched at lower conversions, and the stereochemistry of the recovered enone was analyzed by GLC. As seen in Table 9, **1e** were isomerized in all cases. These results give a clue to the reaction mechanism as will be described later.

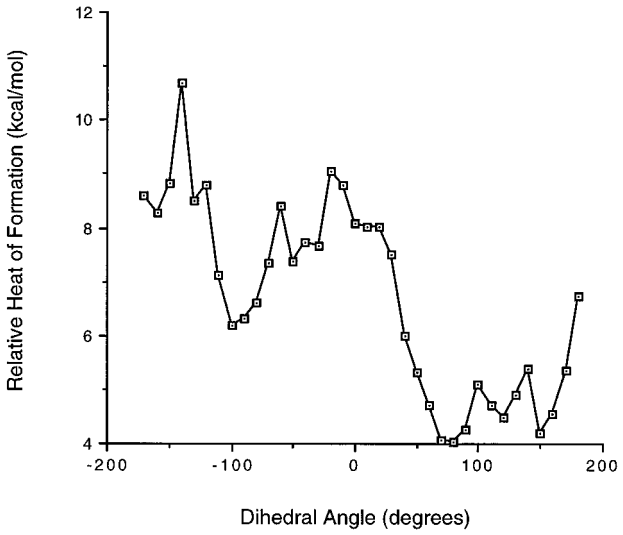


Figure 2. Change of the enthalpy of reaction between **4a** and Ph(CO)CH=CH_2−$SnCl_4$ in terms of the dihedral angle (ϕ). The sum of the ΔH_f values of the reactants is taken as zero.

MO Calculations for Nucleophilic Process. The semiempirical MO calculations have been generally considered the method of choice for studying the structures and energies of transition states of complicated systems, otherwise impossible to tackle by *ab initio* calculations.[15,16] In the hope of obtaining better insight into the nucleophilic mechanism, we invoked the theoretical calculations at the restricted Hartree−Fock (RHF) level using the PM3 semiempirical SCF-MO method[16−18] for the transitions states in the $SnCl_4$-catalyzed nucleophilic reaction of ketene silyl acetals with α-enones. First, the reaction **4a** and Ph(CO)CH=CH_2−$SnCl_4$ complex was analyzed. The activation enthalpy ($\Delta H^{\ddagger}$) is evaluated as the difference in the ΔH_f (heat of formation) values of the reaction pair from the sum of the ΔH_f values of reactants. The $\Delta H^{\ddagger}$ is plotted against the dihedral angle formed by the approaching two C=C bonds (ϕ) at a fixed bond distance between the two reacting centers (2.11 Å) as shown in Figure 2. There appear seven minima, each of which corresponds to different transition state geometries when the bond distance between the two reacting centers is varied. Several transition state geometries are feasible in this reaction for cases where both reaction centers are not congested. By the same method, the reactions between **2a** and **1a**−$SnCl_4$ and between **4a** and **1a**−$SnCl_4$ were compared (the reaction given as entry 2 in Table 1). In these cases, there also appeared several minima by changing the dihedral angle (Figure 3); however, one of them in each case (A an B) is appreciably lower in energy than the others, indicative of being the transition states with fixed geometries. The

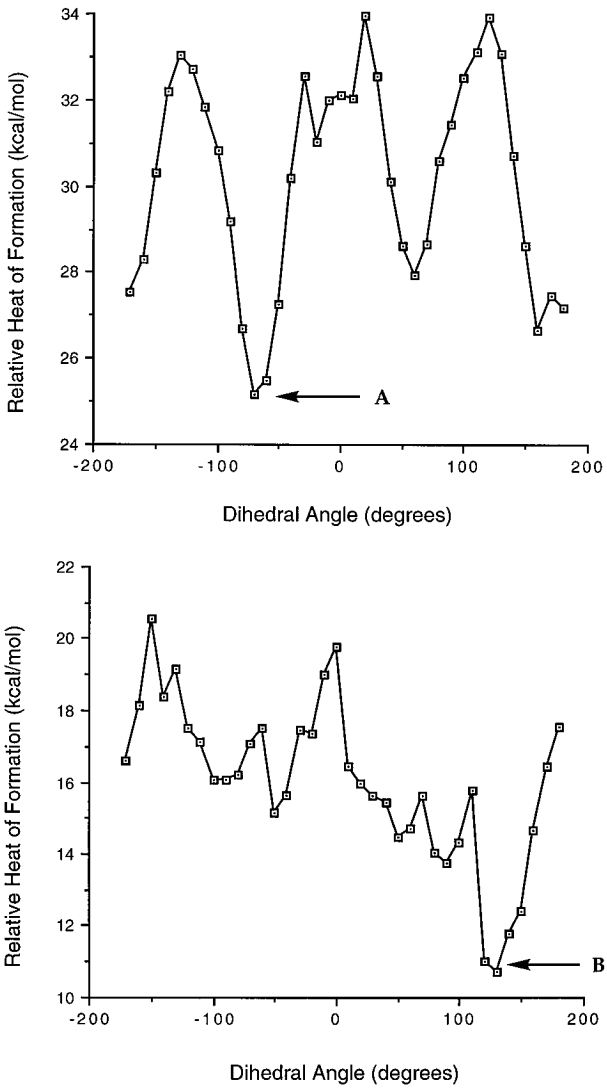


Figure 3. Change of the enthalpy of reactions between **2a** and **1a**−$SnCl_4$ (upper) and between **4a** and **1a**−$SnCl_4$ (lower) in terms of the dihedral angle (ϕ).

reaction coordinate energy profiles of these transition states in terms of the bond distance between the reacting centers are shown in Figure 4.[19] The structures of the transition states A and B are illustrated in Figure 5. The stationary points on the reaction coordinate energy profiles were well characterized as the transition states by calculating and diagonalizing the Hessian matrix which had only one negative eigenvalue (see Experimental Section). The $\Delta H^{\ddagger}$ value of the reaction with **2a** (A: 24.7 kcal mol^{-1}) is significantly larger than that with **4a** (B: 10.1 kcal mol^{-1}) by 14.6 kcal/mol (Figure 4). The activation entropy ($\Delta S^{\ddagger}$) is also evaluated as the difference in the ΔS values of the reaction pair from the sum of the ΔS values of the reactants. The activation free energy ($\Delta G^{\ddagger} = \Delta H - T\Delta S^{\ddagger}$) of **2a** is also significantly larger than that of **4a** by 13.6 kcal mol^{-1}.[20,21] These calculations suggest that nucleophilic attack by less substituted ketene silyl acetals should be orders of

(15) (a) Dewar, M. J. S.; Healy, E. F.; Stewart, J. J. P. *J. Chem. Soc. Faraday Trans. 2* **1984**, *80*, 227. (b) Saá, J. M.; Deyá, P. M.; Suñer, G. A.; Frontera, A. *J. Am. Chem. Soc.* **1992**, *114*, 9093 and references cited therein.

(16) The PM3 semiempirical calculations have been shown to be highly useful for predicting the transition-state structures of reactions of organic compounds containing heteroatoms. See: Alnajjar, M. S.; Franz, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 1052.

(17) The PM3 calculations were carried out using the MOPAC Molecular Orbital Program Package, QCPE 455 (Ver. 6.0), Quantum Chemistry Program Exchange, Department of Chemistry, Indiana University, Bloomington, IN. (a) Stewart J. J. P. *J. Comput. Chem.* **1989**, *10*, 209 and 221. (b) Dewar, M. J. S. *J. Comput. Chem.* **1990**, *11*, 541. (c) Stewart, J. J. P. *J. Comput. Chem.* **1990**, *11*, 543.

(18) It was confirmed that fully optimized *ab initio* SCF-MO calculation using the 3-21 G basis set gave essentially the same structure of the α-enone−$SnCl_4$ complex as the PM3 calculation (see Experimental Section).

(19) Since the calculations for the reaction coordinate are performed by optimizing the total molecular energy with respect to all structural variables, the dihedral angles of the transition states (Figures 5a and 5b) are somewhat different from those of minima at a fixed bond distance between the two reacting centers in Figure 3.

(20) The ΔS values were calculated at 298 K. The inclusion of entropy term results in no significant change in the relative difference in the transition state energies of **4a** and **2a**.

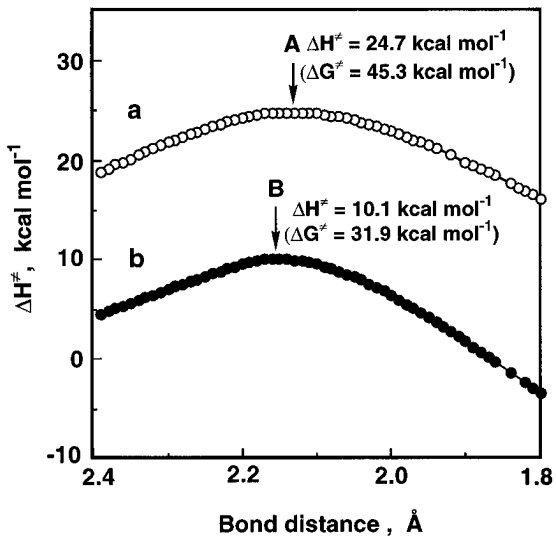
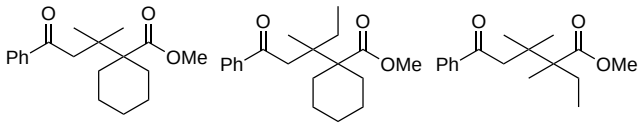


Figure 4. Reaction coordinate energy profiles of the transition states A and B.

magnitude faster than those of more substituted. This stands in sharp contrast to the experimental observations.

Connection of Contiguous Quaternary Carbon Centers. Another important synthetic aspect to be emphasized in relation to the present process is its ability to construct structures with contiguous quaternary carbon centers, a challenging task for synthetic chemists.[22] Although Michael reactions hold great promise for this purpose, conventional lithium enolate methodologies fail to give satisfactory results.[23] For example, Dauben et al. utilized a high pressure technology to connect potential quaternary carbon centers, but succeeded only with activated enolates.[24] Casey revealed that a chromium vinylcarbene complex worked as a Michael acceptor.[25] Holton employed acceptors doubly substituted by electron-withdrawing groups.[26] Nonetheless, these methods suffer from various problems such as low yields, difficulties in preparing raw materials, and tedious procedures. Obviously, the easy preparation of Michael adducts disclosed above proves the Mukaiyama−Michael reaction to be highly promising. In fact, Mukaiyama has already shown some simple examples along this line,[27] but the versatility of this method has not been fully recognized. It should be noted that successful preparation of compounds **5i**−**k** broadens the scope of this method.



5i (93%) **5j** (92%) **5k** (97%)

Discussion

Mayr has broadly assessed the reactivity of π-nucleophiles.[4] Although the effect of β-substituents in ketene silyl acetals on their nucleophilicity is not apparent, the comparison with trimethylsilyl allylic compounds with methyl group(s) at the γ-positions is given: the nucleophilicity parameter (N) varies from 1.62 (allyltrimethylsilane) to 1.73−1.99 (crotyltrimethylsilane) and 0.84 (prenyltrimethylsilane). Evidently, monomethyl substitution increases the nucleophilicity slightly, but dimethyl substitution decreases half the reactivity. Accordingly, the enhanced reactivity of ketene silyl acetals with more β-substituents in the Mukaiyama−Michael reaction is incompatible with the conventional nucleophilic mechanism (Table 1−3). In fact, RajanBabu found that reaction of an equimolar mixture of β,β-disubstituted and β-monosubstituted ketene silyl acetals with cyclopentenone gave the Michael adducts derived from both ketene silyl acetals in ca. 1:1 ratio under thermal conditions where the nucleophilic reaction is likely to proceed.[28] Since the facile connection of more hindered sites is characteristic of radical reactions, we propose the mechanism involving radical coupling that is shown representatively for the $SnCl_4$-mediated reaction in Scheme 3. The initial step is electron transfer from ketene silyl acetal to $SnCl_4$ to generate a cation radical of the ketene silyl acetal and an $SnCl_4$ anion radical. The $SnCl_4$ anion radical spontaneously decomposes to $SnCl_3$ radical and Cl^-. The $SnCl_3$ radical reacts with an α-enone in a 1,4-fashion to give a stannyl enolate radical which subsequently couples with the cation radical to give a stannyl enolate of the Michael adduct. Transmetalation of this intermediate with in situ-formed trialkylsilyl chloride produces the corresponding silyl enol ether and regenerates $SnCl_4$.

The results of the reaction of ketene silyl acetals with $TiCl_4$ (Table 5) and $SnCl_4$ (Table 6) are consistently accounted for in terms of electron transfer. As Reetz et al.[2a] and Rhodes et al.[2b] suggested, an electron transfer from ketene silyl acetal to $TiCl_4$ to give an ester radical, $TiCl_3$ radical, and Cl^-. $TiCl_3$ radical may combine with the ester radical but the titanium−carbon bond is so thermally labile that titanium binds oxygen to generate a titanium enolate. Alternatively, direct homo coupling of the ester radical is also feasible without passing through the titanium enolate intermediate. Analogous electron transfer from $SnCl_4$ produces an $SnCl_3$ radical that couples with the ester radical to afford the thermally stable α-stannyl esters. Thus, both of the above reactions can be explained by an initial electron transfer and the discrepancy of the reaction course can be ascribed straightforwardly to the difference in metal−carbon bond character.

The suppression of the reaction with increasing amounts of $SnCl_4$ (Table 7) is also incompatible with the nucleophilic mechanism where the increase in the amount of Lewis acid should afford higher yields or at least depression of the yield should not occur. The concentration of free $SnCl_4$ that is not coordinated with α-enone may increase with an increase in the $SnCl_4$ concentration. In such a case, electron transfer from ketene silyl acetal to free $SnCl_4$ may compete with that to the $SnCl_4$−α-enone complex, resulting in the formation of α-stannyl ester via the coupling of the ester radical and $SnCl_3$ radical in

(21) The $\Delta G^{\ddagger}$ value of the reaction between **4a** and Ph(CO)-CH=CH_2−$SnCl_4$ complex, where the reaction center is least congested, is also evaluated as 19.6 kcal mol^{-1} ($\Delta H^{\ddagger}$ = 3.2 kcal mol^{-1}), which is the smallest among these reactions.

(22) For relevant studies, see literatures cited in ref 6.

(23) Oare, D. A.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 132.

(24) Dauben, W. G.; Gerdes, J. M. *Tetrahedron Lett.* **1983**, *24*, 3841. Dauben, W. G.; Bunce, R. A. *J. Org. Chem.* **1983**, *48*, 4642.

(25) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391.

(26) Holton, R. A.; Williams, A. D.; Kennedy, R. M. *J. Org. Chem.* **1986**, *51*, 5482.

(27) Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1976**, 163. Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1986**, 1805. Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1987**, 1183. Hashimoto, Y.; Sugumi, H.; Okauchi, T.; Mukaiyama, T. *Chem. Lett.* **1987**, 1691. Minowa, N.; Mukaiyama, T. *Chem. Lett.* **1987**, 1719. Kobayashi, S.; Tamura, M.; Mukaiyama, T. *Chem. Lett.* **1988**, 91.

(28) RajanBabu, T. V. *J. Org. Chem.* **1989**, *49*, 2083.

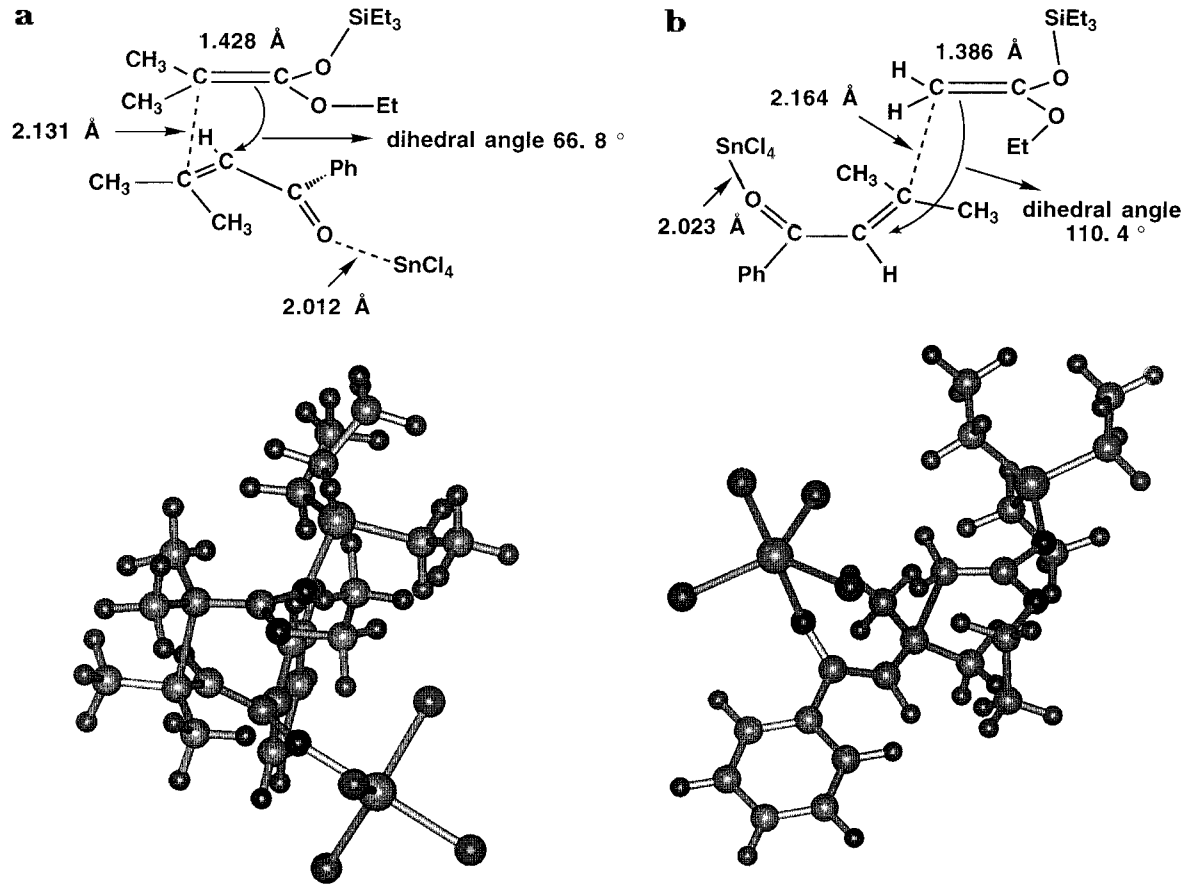
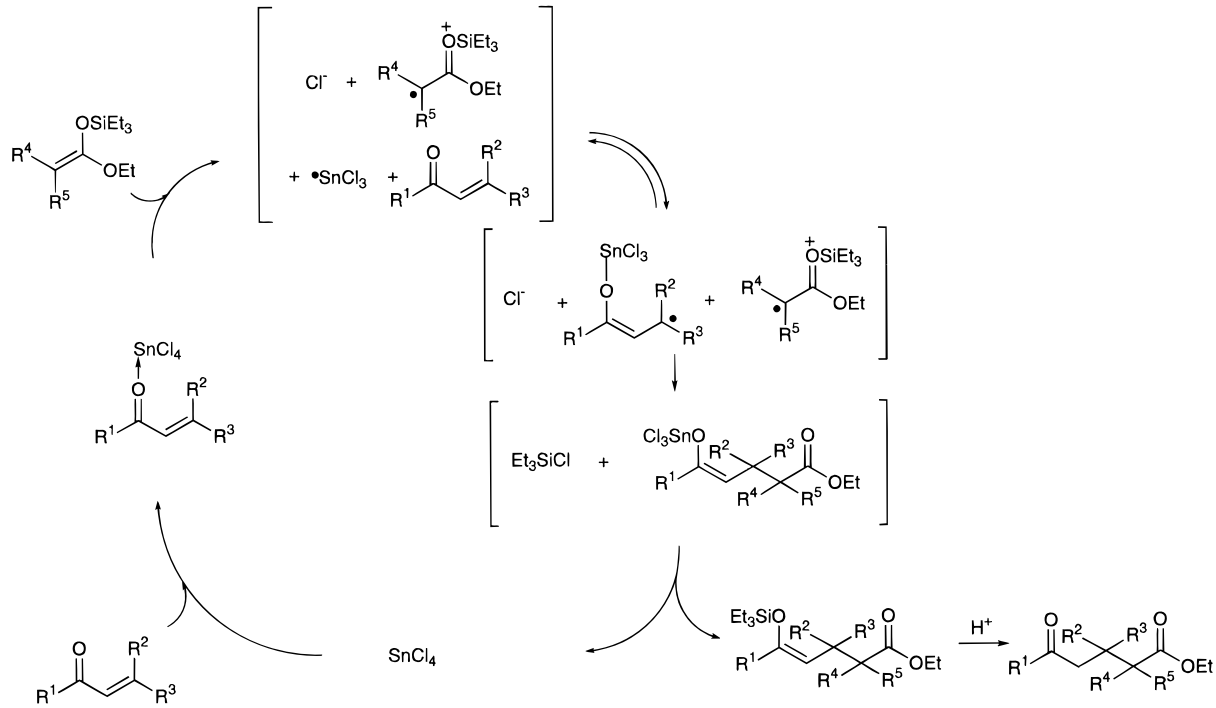


Figure 5. (a) Transition state structure of A. (b) Transition state structure of B.

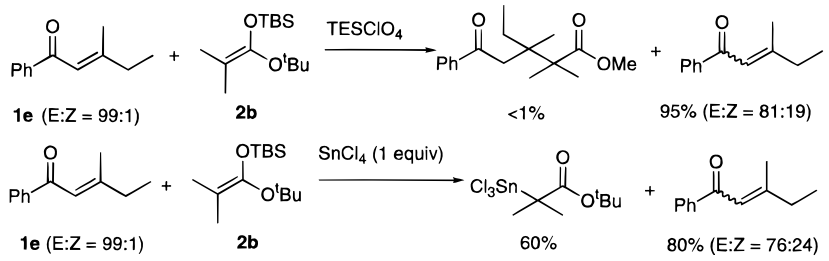
Scheme 3



competition with the formation of the Michael adduct. It was confirmed that no reaction occurred between the α-stannyl ester and α-enone. No suppression of the Michael reaction was observed by use of the stoichiometric $TiCl_4$. The large formation constant for the $TiCl_4$–α-enone complex as compared with that for the $SnCl_4$–α-enone complex (Figure 1) accounts well for such differences between $SnCl_4$ and $TiCl_4$.

The ketene silyl acetals with bulky group(s) exhibit the normal selectivity that is deduced from the nucleophilic process (Table 1–3). The nucleophilic reaction leading to such selectivity is shown in the reaction employing $LiClO_4$ (Scheme 1) and Et_2AlCl (Scheme 2), both of these Lewis acids being incapable of working as an electron acceptor. We have previously disclosed that the bulky ketene silyl acetals are less readily oxidized than the

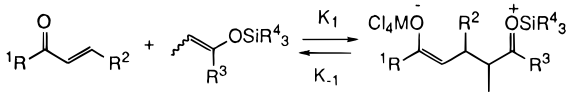
Scheme 4



corresponding less bulky analogs.[3] Thus, the competition reaction employing *O,S*-ketene silyl acetals is noteworthy since the oxidation potentials of these compounds are higher than those of the *O,O*-analogs and even greater than those of the bulky ketene silyl acetals involving TBS and ^{t}BuO groups.[3] In line with this, *O,S*-acetals gave rise to the normal selectivity (Table 4).

In the competition reactions between less bulky ketene silyl acetals, the preference for the more hindered Michael adducts was best achieved in the order $SnCl_4$ > Et_3SiClO_4 > $TiCl_4$. On the other hand, the opposite order is found for the less hindered adducts with bulky ketene silyl acetals. These results are interpreted on the basis of strong oxophilicity of $TiCl_4$. The reduction potential of $TiCl_4$ may be decreased by the strong coordination with α-enone, and thus the electron-transfer pathway of less bulky ketene silyl acetals may be retarded to some extent, resulting in the worst selectivity. By contrast, the electron transfer is most efficiently suppressed in the $TiCl_4$-promoted reaction of less oxidizable bulky ketene silyl acetals since $TiCl_4$ is no longer a good electron acceptor due to tight complexation.

In the electron-transfer initiated pathway in Scheme 3 which involves the equilibrium step, it is presumed that the double bond of an α-enone might be isomerized during the reaction. This is indeed the case (Table 9). Such isomerization may also be envisioned to occur in the nucleophilic process (eq 4). However, this possibility has already been ruled out by Heathcock et al.; while k_1 and k_{-1} are comparable with enol silyl ethers (R′ = alkyl), the reaction of strongly nucleophilic ketene silyl acetals (R′ = alkoxyl) has an early transition state, biasing the equilibrium to the right ($k_1 \gg k_{-1}$).[29] This is consistent with our previous study on designing a diastereoselective Michael reaction.[30] If the equilibrium (eq 4) exists, the reverse reaction should prevail for the bulkier ketene silyl acetals more than for the less bulky ones, leading to lower diastereoselectivity. The experimental outcome, however, is completely opposite; the high diastereocontrol (up to >99:1 syn selectivity) is attained in reaction 4 when R^3 is a bulky alkoxy group and R^4_3 = ^{t}BuMe$_2$. Such high stereoselectivity is otherwise not observed. Hence, it is reasonably concluded that the double bond isomerization of α-enone is not caused by the equilibrium (eq 4) of the nucleophilic process.



(4)

Reaction of β-monomethyl-substituted derivative **3a** also led to isomerization. Notably, the Michael adducts showed low diastereoselectivity which might be caused by involvement of the electron transfer process. (The relative stereochemistry was not determined.)

$TiCl_4$ promotes a variety of reactions. However, reaction between **1a** and **2b** afforded only a 10% yield of the desired Michael adduct together with the recovered **1a** (80%) (Scheme 4). While one might be tempted to attribute the poor yield to the homo coupling of **2b**, this is not the case; no succinate was detected. We reason that electron transfer from **2b** to $TiCl_4$ is suppressed in the presence of α-enone as described above. An alternative nucleophilic reaction between sterically crowded latent quaternary centers would be difficult. When **1e** was exposed to bulky **2b** in the presence of Et_3SiClO_4, only isomerization of **1e** occurred. Remarkably, when the reaction was conducted in the presence of $SnCl_4$, an α-stannyl ester (60%) was produced in addition to the isomerized α-enone. This contrasts with $TiCl_4$ that failed to provide the succinate in the analogous reaction between **2b** and **1a**. Obviously, the α-stannyl ester did not result from the direct transmetalation between **2b** and $SnCl_4$, but the α-enone **1e** was involved in the enolate exchange process. These results again lend support to the facile electron transfer in $SnCl_4$- and $TESClO_4$-mediated reactions. The failure of the Michael reaction implies that sterically demanding reaction centers do not readily undergo radical coupling.

Conclusion

The course of the Mukaiyama−Michael reaction has proven to be highly dependent on ketene silyl acetal and Lewis acid. We interpret these results in the following way. The reaction is usually initiated by electron transfer from ketene silyl acetal to Lewis acid. The reduced Lewis acid radical species attacks α-enone to give an enolate radical, which combines with a cation radical derived from the ketene silyl acetal. However, a competing nucleophilic reaction pathway intervenes when the following conditions are fulfilled: (1) A ketene silyl acetal contains bulky substituents, which increase the ionization potential of the compound in solution. (2) The Lewis acid should be sufficiently oxygenophilic to form a tight complex with α-enone. It should be noted again that the competition reactions serve well for probing the reaction mechanism.

Experimental Section

All solvents were purified by standard methods before use. Ketene silyl acetals were prepared according to literature methods.[31] Reagent-grade $SnCl_4$ and $TiCl_4$ were used as received. Preparation of $Bu_2Sn(OTf)_2$[32] and $TESClO_4$[33] was described in the literature.

(29) Heathcock, C. H.; Norman, M. H.; Uehling, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 2797.

(30) Otera, J.; Fujita, Y.; Sato, T.; Nozaki, H.; Fukuzumi, S.; Fujita, M. *J. Org. Chem.* **1992**, *57*, 5054.

(31) Ireland, R. E.; Wipf, P.; Armstrong, J. D., III *J. Org. Chem.* **1991**, *56*, 650. Otera, J.; Fujita, Y.; Fukuzumi, S. *Synlett* **1994**, 213. Gennari, C.; Beretta, M. G.; Bernardi, A.; Moro, G.; Scolastico, C.; Todeschini, R. *Tetrahedron* **1986**, *42*, 893.

(32) Sato, T.; Otera, J.; Nozaki, H. *J. Am. Chem. Soc.* **1990**, *112*, 901.

Preparation of 1. To a THF solution (200 mL) of diisopropylamine (24.3 g, 0.24 mol) at 0 °C was added a 2.5 M solution of butyllithium in hexane (96 mL, 0.24 mol). After 10 min, the solution was cooled to −78 °C and acetophenone (24.0 g, 0.2 mol) was added over a 5 min period by syringe. After 2.5 min, HMPA (40 mL) was added. After 5 min, trimethylsilyl chloride (26.1 g, 0.24 mol) was added over a 30 s period. The solution was warmed to room temperature (30 min), diluted with cold pentane, and washed three times with ice cold water. The organic layer was then washed with saturated brine and dried over Na_2SO_4. The solvent was removed with a rotary evaporator, and the resulting crude product was purified by distillation with a Kugelrohr apparatus (bath temperature, 90 °C/60 mmHg) to give 1-phenyl-1-(trimethylsiloxy)ethene (31.1 g, 81%). To a CH_2Cl_2 solution (200 mL) of **8d** (45.5 g, 0.24 mol) was added acetone (11.0 g, 0.19 mol) at −78 °C. After 1 min, 1-phenyl-1-(trimethylsiloxy)-ethene (31.1 g, 0.16 mol) was added. The solution was stirred at −78 °C for 3 h. The reaction mixture was extracted with EtOAc. The organic layer was washed with $NaHCO_3$ solution and brine and then dried (Na_2SO_4). After evaporation, the resulting crude product was purified by distillation with a Kugelrohr apparatus (bath temperature, 110 °C/60 mmHg) to give $C_6H_5COCH_2C(OH)(CH_3)_2$ (22.0 g, 77%). To a CH_2Cl_2 solution (100 mL) of this compound (21.98 g, 0.12 mol) was added Et_3N (36.4 g, 0.36 mol) at 0 °C. To this solution was added $(CF_3CO)_2O$ (37.8 g, 0.18 mol). The solution was stirred at 0 °C for 10 min, and allowed to warm up to room temperature. After 1 h, the reaction mixture was extracted with CH_2Cl_2. The organic layer was washed with $NaHCO_3$ solution and brine and dried (Na_2SO_4). The solvent was removed to give crude $C_6H_5COCH_2C(OCOCF_3)(CH_3)_2$. To a C_6H_6 solution (100 mL) of this compound (crude product, 0.12 mol) was added DBU (23.8 g, 0.16 mol) at room temperature. The solution was stirred at room temperature for 1.5 h. The reaction mixture was extracted with C_6H_6. The organic layer was washed with cold 1 N HCl, cold $NaHCO_3$ solution, and brine and dried (Na_2SO_4). Evaporation and column chromatography on silica gel (95:5 hexane−EtOAc) afforded **1a** (13.5 g, 70%): ^{1}H NMR δ 2.01 (s, 3H), 2.02 (s, 3H), 6.75 (s, 1H), 7.42−7.53 (m, 3H), 7.92 (d, 2H, J = 7.69 Hz); ^{13}C NMR δ 20.81, 27.60, 120.83, 127.84, 128.11, 131.93, 138.94, 156.27, 190.97; MS (m/z) 161 ($M^+ + 1$); HRMS calcd for $C_{11}H_{12}O$ (M^+) 160.0880, found 160.0871. By an analogous procedure, **1e** was obtained. Column chromatography of the E/Z mixture on silica gel (98:2 hexane−EtOAc) provided (*Z*)-**1e** as the first fraction and the (*E*)-isomer as the second one. (*Z*)-**1e**: ^{1}H NMR δ 1.13 (t, 3H, J = 7.51 Hz), 2.00 (s, 3H), 2.63 (q, 2H, J = 7.51 Hz), 6.70 (s, 1H), 7.42−7.53 (m, 3H), 7.93 (d, 2H, J = 7.33 Hz). (*E*)-**1e**: ^{1}H NMR δ 1.53 (t, 3H, J = 7.33 Hz), 2.19 (s, 3H), 2.28 (q, 2H, J = 7.33 Hz), 6.72 (s, 1H), 7.42−7.54 (m, 3H), 7.63 (d, 2H, J = 7.33 Hz); MS (m/z) 174 (M^+); HRMS calcd for $C_{12}H_{14}O$ (M^+) 174.1045, found 174.1037.

To a THF solution (200 mL) of diisopropylamine (24.3 g, 0.24 mol) was added 2.5 M solution of butyllithium in hexane (96 mL, 0.24 mol) at −78 °C. After 15 min, pinacolone (20.0 g, 0.2 mol) was added. After 30 min, acetaldehyde (10.6 g, 0.24 mol) was added. The reaction mixture was stirred at −78 °C for 3 h. The reaction was quenched by adding NH_4Cl solution. The reaction mixture was extracted with Et_2O. The organic layer was washed with NH_4Cl solution and brine and then dried (Na_2SO_4). The solvent was removed, and the resulting crude product was purified by distillation with a Kugelrohr apparatus (bath temperature, 100 °C/100 mmHg) to give ^{t}BuCOCH$_2$CH(OH)CH$_3$ (21.1 g, 73%). To a CH_2Cl_2 solution (100 mL) of this compound (21.1 g, 0.15 mol) was added Et_3N (44.5 g, 0.44 mol) at 0 °C. To this solution was added $(CF_3CO)_2O$ (46.0 g, 0.22 mol). The solution was stirred at 0 °C for 10 min and allowed to warm to room temperature. After 1 h, the reaction mixture was extracted with CH_2Cl_2. The organic layer was washed with $NaHCO_3$ solution and brine and dried (Na_2SO_4). The solvent was removed to give crude ^{t}BuCOCH$_2$CH(OCOCF$_3$)CH$_3$. To a C_6H_6 solution (100 mL) of this compound (crude product, 0.15 mol) was added DBU (28.9 g, 0.19 mol) at room temperature. The solution was stirred at room temperature for 1.5 h. The reaction mixture was extracted with C_6H_6. The organic layer was washed with cold 1 N HCl, cold $NaHCO_3$ solution, and brine and dried (Na_2SO_4). Evaporation and column chromatography on silica gel (95:5 hexane−EtOAc) afforded **1c** (14.9 g, 81%): ^{1}H NMR δ 1.12 (s, 9H), 1.87 (d, 3H, J = 6.96 Hz), 6.50 (dq, 1H, J = 15.92, 1.63 Hz), 6.93 (dq, 1H, J = 15.92, 6.81 Hz); MS (m/z) 126 (M^+); HRMS calcd for $C_8H_{14}O$ (M^+) 126.1045, found 126.1044.

To a suspension of $AlCl_3$ (40.0 g, 0.30 mol) in C_6H_6 (150 mL) was added propionyl chloride (25.9 g, 0.28 mol) at 0 °C. The mixture was stirred for 15 min at room temperature. The reaction mixture was quenched with 200 mL of cold 2 N HCl. The resulting solution was extracted with Et_2O (140 mL × 3). The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (50 mL × 2) and 50 mL of brine and then dried over anhydrous Na_2SO_4. Evaporation and column chromatography of the residue on silica gel (95:5 hexane−EtOAc) afforded **1d** (31.2 g, 76%): ^{1}H NMR δ 2.00 (d, 3H, J = 8.24 Hz), 6.91 (dq, 1H, J = 15.30, 1.44 Hz), 7.08 (dq, 1H, J = 15.30, 7.08 Hz), 7.43−7.56 (m, 3H), 7.92 (d, 2H, J = 8.06 Hz); MS (m/z) 147 ($M^+ + 1$); HRMS calcd for $C_{10}H_{10}O$ (M^+) 146.1906, found 146.0720. Analogous procedure provided **1b**: ^{1}H NMR δ 1.14 (s, 9H), 1.91 (s, 3H), 2.11 (s, 3H), 6.31 (s, 1H); ^{13}C NMR δ 20.63, 26.45, 27.80, 43.42, 119.59, 154.96, 205.85; MS (m/z) 141 ($M^+ + 1$); HRMS calcd for $C_9H_{16}O$ (M^+) 140.1201, found 140.1193.

Michael Reaction. A typical procedure is as follows. To a suspension of **8a** (26.6 mg, 0.05 mmol) in CH_2Cl_2 (5 mL) were added **1a** (160.2 mg, 1.0 mmol) and **2a** (226.6 mg, 1.3 mmol) at −78 °C. The resulting clear solution was stirred for 4 h at this temperature. The reaction mixture was combined with $NaHCO_3$ solution and EtOAc. The organic layer was washed with $NaHCO_3$, 1 N HCl, and brine and then dried (Na_2SO_4). Evaporation and column chromatography of the residue on silica gel (98:2 hexane−EtOAc) afforded **5a** (258 mg, 99%): ^{1}H NMR δ 1.06 (s, 6H), 1.22 (s, 6H), 1.29 (t, 3H, J = 7.33 Hz), 3.07 (s, 2H), 4.16 (q, 2H, J = 7.33 Hz), 7.43−7.56 (m, 3H), 7.93 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 14.08, 21.07, 22.44, 38.53, 43.31, 48.95, 60.22, 128.12, 128.34, 132.58, 138.76, 176.70, 200.72; MS (m/z) 276 (M^+); HRMS calcd for $C_{15}H_{19}O_2$ (M^+ − OEt) 231.1385, found 231.1391. Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.79; H, 9.00.

When ketene silyl acetals derived from *tert*-butyl esters were employed, the crude reaction mixture, which consisted of the *tert*-butyl ester and the corresponding carboxylic acid,[29] was stirred in 5 N HCl/THF at room temperature for 5 h. The mixture was extracted with ether and the organic layer was dried (Na_2SO_4). To this solution was added dropwise diazomethane in ether until the color of this reagent began to persist. Evaporation and column chromatography on silica gel afforded the corresponding methyl esters of the Michael adducts (**5d**, **6d**, and **7d**).

Other reactions were carried out analogously. **5b**: ^{1}H NMR δ 1.08 (s, 6H), 1.11 (s, 9H), 1.14 (s, 6H), 1.27 (t, 3H, J = 7.13 Hz), 2.61 (s, 2H), 4.12 (q, 2H, J = 7.13 Hz); MS (m/z) 257 ($M^+ + 1$); HRMS calcd for $C_{13}H_{23}O_2$ (M^+ − OEt) 211.1698, found 211.1776. Anal. Calcd for $C_{15}H_{28}O_3$: C, 70.27; H, 11.01. Found: C, 70.59; H, 11.34.

5c: ^{1}H NMR δ 0.79 (d, 3H, J = 5.98 Hz), 1.11 (s, 9H), 1.11 (s, 6H), 1.23 (t, 3H, J = 7.12 Hz), 2.31−2.46 (m, 3H), 4.11 (q, 2H, J = 7.12 Hz); MS (m/z) 243 ($M^+ + 1$); HRMS calcd for $C_{12}H_{21}O_2$ (M^+ − OEt) 197.1542, found 197.1556. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.50; H, 11.09.

5d: ^{1}H NMR δ 0.72 (d, 3H, J = 6.22 Hz), 1.05 (s, 9H), 1.06 (s, 6H), 2.29−2.36 (m, 3H), 3.58 (s, 3H); ^{13}C NMR δ 14.98, 21.61, 22,34, 26.08, 35.23, 38.97, 45.11, 51.33, 177.75, 214.23; MS (m/z) 229 ($M^+ + 1$); HRMS calcd for $C_{12}H_{21}O_2$ (M^+ − OMe) 197.1542, found 197.1561. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.76; H, 10.86.

5e: ^{1}H NMR δ 0.80−0.95 (m, 13H), 1.05−1.37 (m, 17H), 1.65−1.77 (m, 2H), 1.92−2.00 (m, 1H), 2.31−2.49 (m, 4H), 4.80−4.85 (m, 1H); MS (m/z) 350 (M^+); HRMS calcd for $C_{22}H_{38}O_3$ (M^+) 350.2821, found 350.2819. Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.21; H, 11.04.

(33) Lambert, J. B.; McConnell, J. A.; Schiff, W.; Schultz, W. J., Jr. *J. Chem. Soc., Chem. Commun.* **1988**, 455.

5f: ^{1}H NMR δ 0.89 (d, 3H, J = 6.52 Hz), 1.19 (s, 6H), 1.25 (t, 3H, J = 7.13 Hz), 2.52−2.77 (m, 2H), 2.96−3.02 (m, 1H), 4.14 (q, 2H, J = 7.12 Hz), 7.43−7.56 (m, 3H), 7.95 (d, 2H, J = 7.08 Hz); MS (m/z) 262 (M^+). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.60; H, 8.75.

5g: ^{1}H NMR δ 1.05 (s, 6H), 1.23 (s, 6H), 3.06 (s, 2H), 3.70 (s, 3H), 7.43−7.56 (m, 3H), 7.93 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 21.13, 22.50, 38.63, 43.33, 49.18, 51.41, 128.18, 128.42, 132.66, 138.77, 177.25, 200.70; MS (m/z) 262 (M^+); HRMS calcd for $C_{15}H_{19}O_2$ (M^+ − OMe) 231.1385, found 231.1355. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.15; H, 8.68.

5h: ^{1}H NMR δ 0.80 (t, 3H, J = 7.33 Hz), 1.05 (s, 3H), 1.17−1.21 (m, 9H), 1.52−1.79 (m, 2H), 3.10 (ABq, 2H, J = 17.75 Hz, $\Delta\nu_{AB}$ =27.27 Hz), 4.06 (q, 2H, J = 7.33 Hz), 7.40−7.52 (m, 3H), 7.94 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 9.75, 13.99, 20.86, 21.97, 27.97, 41.26, 41.85, 49.23, 60.24, 127.96, 128.38, 132.46, 138.75, 177.07, 200.50; MS (m/z) 290 (M^+); HRMS calcd for $C_{16}H_{21}O_2$ (M^+ − OEt) 245.1542, found 245.1472. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.44; H, 9.02. Found: C, 74.81; H, 9.21.

5i: ^{1}H NMR δ 1.02 (s, 6H), 1.22−2.21 (m, 10 H), 2.98 (s, 2H), 3.72 (s, 3H), 7.42−7.56 (m, 3H), 7.91 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 22.83, 24.07, 25.51, 28.70, 39.14, 43.27, 51.01, 54.72, 128.15, 128.38, 132.61, 138.83, 175.46, 200.82; MS (m/z) 302 (M^+); HRMS calcd for $C_{15}H_{18}O_3$ (M^+ − C_4H_8)246.1256, found 246.1238. Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.15; H, 8.79.

5j: ^{1}H NMR δ 0.82 (t, 3H, J = 7.33 Hz), 1.05 (s, 3H), 1.11−2.16 (m, 12H), 3.03 (ABq, 2H, J = 16.48 Hz, $\Delta\nu_{AB}$ = 28.54 Hz), 3.63 (s, 3H), 7.42−7.56 (m, 3H), 7.93 (d, 2H, J = 7.33 Hz);^{13}C NMR δ 9.81, 21.27, 24.16, 25,57, 27.84, 29.61, 41.08, 42.67, 51.03, 54.94, 127.93, 128.40, 132.43, 138.74, 175.68, 200.18; MS (m/z) 316 (M^+); HRMS calcd for $C_{18}H_{25}O$ (M^+ − COOMe) 257.1906, found 257.1905. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.91. Found: C, 76.12; H, 9.15.

5k: ^{1}H NMR δ 0.84 (t, 3H, J = 7.33 Hz), 0.98 (s, 3H), 1.09 (s, 3H), 1.16 (s, 3H), 1.35−1.40 (m, 1H), 2.05−2.10 (m, 1H), 3.05 (ABq, 2H, J = 13.29 Hz, $\Delta\nu_{AB}$ = 24.11 Hz), 3.70 (s, 3H), 7.42−7.56 (m, 3H), 7.92 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 9.86, 16.55, 22.79, 25.99, 39.29, 43.31, 51.17, 53.71, 128.15, 128.39, 132.61, 138.79, 176.41, 200.70; MS (m/z) 276 (M^+); HRMS calcd for $C_{16}H_{21}O_2$ (M^+ − OMe) 245.1542, found 245.1577. Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.62; H, 8.92.

6a: ^{1}H NMR δ 1.11 (s, 3H), 1.12 (s, 3H), 1.16 (d, 3H, J = 6.96 Hz), 1.18 (t, 3H, J = 6.96 Hz), 2.76 (q, 1H, J = 6.96 Hz), 2.84−3.22 (m, 2H), 4.09 (q, 2H, J = 6.96 Hz), 7.42−7.56 (m, 3H), 7.94 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 12.33, 14.66, 25.41, 35.70, 45.89, 47.72, 59.96, 128.02, 128.48, 132.76, 138.43, 175.66, 199.79; MS (m/z) 262 (M); HRMS calcd for $C_{16}H_{22}O_3$ (M^+) 262.1569, found 262.1558. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.27; H, 8.73.

6b: ^{1}H NMR δ 1.05 (s, 3H), 1.06 (s, 3H), 1.08 (d, 3H, J = 7.17 Hz), 1.11 (s, 9H), 1.25 (t, 3H, J = 7.17 Hz), 2.40−2.71 (m, 2H), 2.80 (q, 1H, J = 7.17 Hz), 4.10 (q, 2H, J = 7.15 Hz); MS (m/z) 242 (M^+); HRMS calcd for $C_{12}H_{21}O_2$ (M^+ − OEt) 197.1542, found 197.1544. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.02; H, 11.18.

6c: ^{1}H NMR δ 0.75 (d, 3H, J = 5.93 Hz), 1.05−1.10 (m, 3H), 1.07 (s, 9H), 1.19 (t, 3H, J = 7.09 Hz), 2.27−2.42 (m, 4H), 4.07 (q, 2H, J = 7.09 Hz); MS (m/z) 228 [M^+]. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.76; H, 10.86.

6d: ^{1}H NMR δ 0.85 (d, 3H × 0.96, J = 6.54 Hz), 0.87 (d, 3H × 0.04, J = 5.80 Hz), 1.10−1.13 (m, 12H), 2.43−2.46 (m, 4H), 3.66 (s, 3H × 0.04) 3.67 (s, 3H × 0.96); MS (m/z) 214 (M^+); HRMS calcd for $C_{12}H_{22}O_3$ (M^+) 214.1569, found 214.1571.

6e: ^{1}H NMR δ 0.81−0.95 (m, 12H), 1.05−1.35 (m, 14H), 1.60−1.75 (m, 2H), 1.88−2.00 (m, 1H), 2.35−2.64 (m, 6H), 4.84−4.88 (m, 1H); MS (m/z) 337 (M^+ + 1); HRMS calcd for $C_{21}H_{36}O_3$ (M^+) 336.2664, found 336.2655. Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 75.05; H, 10.61.

6f: ^{1}H NMR δ 0.96 (d, 3H × 0.60, J = 6.96 Hz), 0.98 (d, 3H × 0.40, J = 6.59 Hz), 1.16 (d, 3H × 0.60, J = 6.96 Hz), 1.18 (d, 3H × 0.40, J = 6.59 Hz), 2.51−2.61 (m, 2H), 2.75-2.83 (m, 1H), 3.01−3.19 (m, 1H), 3.67 (s, 3H × 0.40), 3.68 (s, 3H × 0.60), 7.44−7.58 (m, 3H), 7.95−7.97 (m, 2H); MS (m/z) 234 (M^+); HRMS calcd for $C_{14}H_{18}O_3$ (M^+) 234.1256, found 234.1267.

6g: ^{1}H NMR δ 0.83 (t, 3H, J = 7.33 Hz), 1.07−1.20 (m, 9H), 1.49−1.76 (m, 2H), 2.83−3.26 (m, 3H), 4.03−4.11 (m, 2H), 7.42−7.56 (m, 3H), 7.95 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 8.14, 11.86, 14.07, 21.49, 29.50, 38.40, 42.67, 45.58, 59.87, 127.86, 128.41, 132.63, 138.45, 175.75, 199.72; MS (m/z) 276 (M^+); HRMS calcd for $C_{15}H_{19}O_2$ (M^+ − OEt) 231.1385, found 231.1354. Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 74.08; H, 8.91.

7a: ^{1}H NMR δ 1.17 (s, 6H), 1.19 (t, 3H, J = 7.33 Hz), 2.53 (s, 2H), 3.11 (s, 2H), 4.08 (q, 2H, J = 7.33), 7.42−7.56 (m, 3H), 7.94 (d, 2H, J = 7.33 Hz); ^{13}C NMR δ 14.19, 28.25, 32.98, 45.05, 47.16, 59.93, 127.97, 128.47, 132.76, 138.24, 172.24, 199.63; MS (m/z) 248 (M^+); HRMS calcd for $C_{15}H_{20}O_3$ (M^+) 248.1412, found 248.1450. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.87; H, 8.36.

7b: ^{1}H NMR δ 1.08 (s, 6H), 1.12 (s, 9H), 1.24 (t, 3H, J = 7.14 Hz), 2.51 (s, 2H), 2.64 (s, 2H), 4.09 (q, 2H, J = 7.14 Hz); MS (m/z) 229 (M^+ + 1); HRMS calcd for $C_{11}H_{19}O_2$ (M^+ − OEt) 183.1385, found 183.1367. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.66; H, 10.87.

7c: ^{1}H NMR δ 0.94 (d, 3H, J = 3.69 Hz), 1.11 (s, 9H), 1.24 (t, 3H, J = 7.14 Hz), 2.13−2.57 (m, 5H), 4.10 (q, 2H, J = 7.14 Hz); MS (m/z) 215 (M^+ + 1); HRMS calcd for $C_{12}H_{22}O_3$ (M^+) 214.1569, found 214.1557.

7d: ^{1}H NMR δ 0.89 (d, 3H, J = 5.89 Hz), 1.06 (s, 9H), 2.11−2.51 (m, 5H), 3.59 (s, 3H); ^{13}C NMR δ 19.73, 25.80, 25.84, 26.03, 40.35, 42.45, 51.09, 172.75, 214.24; MS (m/z) 200 (M^+); HRMS calcd for $C_{11}H_{20}O_3$ (M^+) 200.1413, found 200.1401.

7e: ^{1}H NMR δ 0.80−0.95 (m, 13H), 1.04−1.32 (m, 11H), 1.63−1.78 (m, 2H), 1.86−1.96 (m, 1H), 2.15−2.56 (m, 6H), 4.84−4.87 (m, 1H); MS (m/z) 322 (M^+); HRMS calcd for $C_{20}H_{34}O_3$ (M^+) 322.2508, found 322.2521. Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.54; H, 10.98.

Competition Reaction. To a CH_2Cl_2 solution (5 mL) of **8a** (26.6 mg, 0.05 mmol) was added **1a** (160 mg, 1.0 mmol) at −78 °C. To this solution was added a mixture of **2a** (230 mg, 1.0 mmol) and **4a** (202 mg, 1.0 mmol). The solution was stirred at −78 °C for 4 h. The reaction was quenched by adding $NaHCO_3$ solution. The reaction mixture was extracted with EtOAc. The organic layer was washed with $NaHCO_3$ solution, 1 N HCl, and brine and then dried (Na_2SO_4). GLC analysis of the crude mixture obtained by evaporation showed formation of **5a** in 85% yield while **7a** was not detected. Other competition reactions were carried out analogously. When ketene silyl acetals derived from *tert*-butyl esters were employed, the Michael adducts consisted of the *tert*-butyl esters and the corresponding carboxylic acids. Accordingly, the reaction mixture was treated with HCl and diazomethane (vide supra), and the resulting methyl esters were subjected to GLC analysis. The GLC peaks in the competition reaction were fully confirmed by comparison with separately prepared authentic Michael adducts.

Competition Reaction with $LiClO_4$ in Ether. To an ether solution (5 mL) of $LiClO_4$ (26.6 mg, 0.25 mmol) was added 2-cyclohexen-1-one (48.1 mg, 0.5 mmol) at room temperature. To this solution was added a mixture of **2e** (115.1 mg, 0.5 mmol) and **4d** (101.7 mg, 0.5 mmol). After being stirred at room temperature for 5 h, the solution was poured into hexane (50 mL) containing Et_3N (1 mL). The mixture was filtered, and the filtrate was evaporated. GLC analysis of the crude mixture showed **11** to be formed in 62% yield while **9** was not detected. Other reactions were conducted analogously.

Authentic samples of **9**, **10**, and **11** were prepared by $TiCl_4$-promoted reaction.

9: ^{1}H NMR δ 0.11 (s, 3H), 0.13 (s, 3H), 0.91 (s, 9H), 1.08 (s, 3H), 1.10 (s, 3H), 1.25 (t, 3H, J = 7.12 Hz), 1.45−1.63 (m, 3H), 1.78−1.89 (m, 1H), 1.91−2.07 (m, 2H), 2.52−2.60 (m, 1H), 4.12 (q, 2H, J = 7.12 Hz), 4.67 (br s, 1H); MS (m/z) 326 (M^+). Anal. Calcd for $C_{18}H_{34}O_3Si$: C, 66.21; H, 10.49. Found: C, 66.60; H, 10.69.

10: ^{1}H NMR δ 0.11−0.13 (m, 6H), 0.90 (s, 9H × 0.61), 0.91 (s, 9H × 0.39), 1.09 (d, 3H × 0.61, J = 6.96 Hz), 1.11 (d, 3H × 0.39, J = 7.11 Hz), 1.25 (t, 3H × 0.39, J = 7.14 Hz), 1.26 (t, 3H × 0.61, J = 7.11 Hz), 1.49−1.69 (m, 3H), 1.72−1.81 (m, 1H), 1.94−2.02 (m, 2H), 2,26−2.37 (m, 1H), 2.43−2.53 (m, 1H), 4.09−4.17 (m, 2H), 4.67 (br s, 1H × 0.61), 4.80−4.84 (m, 1H

× 0.39); MS (*m*/*z*) 312 (M^+). Anal. Calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.11; H, 10.28.

11: ^{1}H NMR δ 0.12 (s, 6H), 0.91 (s, 9H), 1.25 (t, 3H, *J* = 7.10 Hz), 1.52−1.65 (m, 2H), 1.68-1.78 (m, 2H), 1.94−2.04 (m, 2H), 2.24 (d, 2H, *J* = 7.51 Hz), 2.60−2.70 (m, 1H), 4.13 (q, 2H, *J* = 7.12 Hz), 4.76−4.78 (m, 1H); MS (*m*/*z*) 298 (M^+); HRMS calcd for $C_{12}H_{21}O_3Si$ (M^+ − ^{t}Bu) 241.1260, found 241.1248. Anal. Calcd for $C_{16}H_{30}O_3Si$: C,64.38; H, 10.13. Found: C, 64.60; H, 10.29.

Competition Reaction of *O*-Silyl Ketene *O,S*-Acetals with 1d. To a CH_2Cl_2 solution (5 mL) of **8b** (26 mg, 0.1 mmol) was added **1d** (160 mg, 0.1 mmol) at −78 °C. To this solution was added a mixture of **12** (232.5 mg, 1.0 mmol) and **13** (218.4 mg, 1.0 mmol). The solution was stirred at −78 °C for 4 h. The reaction was quenched by adding $NaHCO_3$ solution. The reaction mixture was washed with EtOAc. The organic layer was washed with $NaHCO_3$ solution, 1 N HCl, and brine, and then dried (Na_2SO_4). GLC analysis of the crude mixture obtained after evaporation showed formation of **14** in 5% yield and **15** in 82% yield; **14**: ^{1}H NMR δ 0.90 (d, 3H, *J* = 6.35 Hz), 1.18 (s, 3H), 1.19 (s, 3H), 1.45 (s, 9H), 2.57−2.76 (m, 2H), 2.98−3.10 (m, 1H), 7.43−7.55 (m, 3H), 7.96 (d, 2H, *J* = 7.09 Hz); MS (*m*/*z*) 306 (M^+). Anal. Calcd for $C_{18}H_{26}O_2S$: C, 70.55; H, 8.55. Found: C, 70.67; H, 8.63; **15**: ^{1}H NMR δ 0.96 (d, 3H × 0.34, *J* = 6.35 Hz), 1.00 (d, 3H × 0.66, *J* = 6.54 Hz), 1.14 (d, 3H × 0.34, *J* = 6.53 Hz), 1.17 (d, 3H × 0.66, *J* = 6.59 Hz), 1.45 (s, 9H × 0.66), 1.46 (s, 9H × 0.34), 2.52−2.62 (m, 2H), 2.67−2.80 (m, 1H), 3.10−2.23 (m, 1H), 7.42−7.49 (m, 2H), 7.53−7.58 (m, 1H), 7.93−7.97 (m, 2H); MS (*m*/*z*) 292 (M^+). Anal. Calcd for $C_{17}H_{24}O_2S$: C, 69.82; H, 8.27. Found: C, 70.01; H, 8.59.

Reaction of 3 with $TiCl_4$ (8d). To a CH_2Cl_2 solution (5 mL) of **3b** (244 mg, 1.0 mmol) was added a 1 M CH_2Cl_2 solution of **8d** (1.0 mL, 1.0 mmol) at −78 °C. The solution was stirred for 30 min and combined with water. The mixture was extracted with ether. The organic layer was washed with water and dried (Na_2SO_4). The ether solution was filtered and treated with diazomethane to afford the corresponding dimethyl ester. The yield of dimethyl ester was determined on the basis of GLC analysis by comparison with an authentic sample. Other reactions were carried out analogously.

Reaction of Ketene Silyl Acetal with $SnCl_4$ (8b). To a CD_2Cl_2 solution (1 mL) of **8b** (130 mg, 0.5 mmol) was added **2a** (150 mg, 0.5 mmol) at −78 °C. The solution was stirred for 30 min at this temperature. The solution was warmed up to room temperature. A portion of this solution (ca. 0.4 mL) was transferred to a nitrogen-filled NMR sample tube which contained benzene (0.5 mmol) as an internal standard. A ^{1}H NMR spectrum unambiguously showed quantitative formation of ethyl 1-(trichlorostannyl)isobutyrate: ^{1}H NMR (CD_2Cl_2) δ 1.24 (t, 3H, *J* = 7.33 Hz), 1.66 (s, 6H) with satellites induced by Sn: $J_{^{119}Sn-H}$ 201.13 Hz; $J_{^{117}Sn-H}$ 192.33 Hz, quite reasonable values for monoalkyltin trichlorides,[34] 4.20 (q, 2H, *J* = 7.33 Hz). No other signals attributable to byproducts were detected.

Other reactions were conducted analogously. *tert*-Butyl 1-(trichlorostannyl)-isobutyrate: ^{1}H NMR (CD_2Cl_2) δ 1.58 (s, 9H), 1.70 (s, 6H) with $J_{^{119}Sn-H}$ 201.89 Hz; $J_{^{117}Sn-H}$ 192.92 Hz.

Methyl 1-(trichlorostannyl)isobutyrate: ^{1}H NMR (CD_2Cl_2) δ 1.71 (s, 6H) with $J_{^{119}Sn-H}$ 200.97 Hz; $J_{^{117}Sn-H}$ 192.06 Hz, 3.79 (s, 3H).

Ethyl 1-(trichlorostannyl)propionate: ^{1}H NMR (CD_2Cl_2) δ 1.28 (3H, *J* = 7.14 Hz), 1.68 (d, 3H, *J* = 7.51 Hz) with $J_{^{119}Sn-H}$ 206.09 Hz; $J_{^{117}Sn-H}$ 190.95 Hz, 2.54 (q, 1H, *J* = 7.51 Hz), 4.23 (q, 2H, *J* = 7.14 Hz).

tert-Butyl 1-(trichlorostannyl)propionate: ^{1}H NMR (CD_2Cl_2) δ 1.58 (s, 9H), 1.61 (d, 3H, *J* = 7.63 Hz) with $J_{^{119}Sn-H}$ 205.40; $J_{^{117}Sn-H}$ 190.17 Hz, 3.70 (q, 1H, *J* = 7.63 Hz).

Methyl 1-(trichlorostannyl)propionate: ^{1}H NMR (CD_2Cl_2) δ 1.63 (d, 3H, *J* = 7.50 Hz) with $J_{^{119}Sn-H}$ 205.49 Hz; $J_{^{117}Sn-H}$ 190.32 Hz, 3.67 (q, 1H, *J* = 7.50 Hz), 3.76 (s, 3H).

Isolation of Enol Silyl Ether Intermediate. Reaction of **1a** and **2a** in the presence of **8a** was carried out as described above. The reaction mixture, after being stirred for 4 h, was poured into hexane (50 mL) containing Et_3N (1 mL). The mixture was filtered and the filtrate was evaporated. The residue was subjected to column chromatography on ammonia-treated silica gel (98:2 hexane−EtOAc) to give **16a** (215 mg, 56%) together with **5a** (116 mg, 38%). **16a**: ^{1}H NMR δ 0.51 (q, 6H, *J* = 7.96 Hz), 0.88 (t, 9H, *J* = 7.69 Hz), 1.20 (s, 6H), 1.22 (t, 3H, *J* = 6.96 Hz), 1.27 (s, 6H), 4.10 (q, 2H, *J* = 6.96 Hz), 4.70 (s,1H), 7.23−7.27 (m, 3H), 7.29−7.34 (m, 2H); MS (*m*/*z*) 390 (M^+); HRMS calcd for $C_{21}H_{33}O_2Si$ (M^+ − OEt) 345.2250, found 345.2271. Upon acidic hydrolysis, **16a** was converted to **5a**.

When the reaction was conducted in CH_2Cl_2 (4.5 mL)−THF (0.5 mL), **16a** was solely obtained even by aqueous workup.

The other reactions were carried out analogously. **16b**: ^{1}H NMR δ 0.01 (s, 9H), 1.19 (s, 6H), 1.22 (s, 6H), 3.63 (s, 3H), 4.76 (s, 1H), 7.21−7.26 (m, 3H), 7.29−7.31 (m, 2H); MS (*m*/*z*) 334 (M^+); HRMS calcd for $C_{16}H_{21}O_3$ (M^+ − Me_3Si) 261.1491, found 261.1575.

16c: ^{1}H NMR δ 0.53 (q, 6H, *J* = 8.06 Hz), 0.90 (t, 9H, *J* = 8.06 Hz), 1.15 (d, 3H, *J* = 6.96 Hz), 1.25 (t, 3H, *J* = 7.33 Hz), 1.27 (s, 6H), 2.80 (q, 1H, *J* = 6.96 Hz), 4.10 (q, 2H, *J* = 7.33 Hz), 4.68 (s, 1H), 7.23−7.34 (m, 5H); MS (*m*/*z*) 376 (M^+); HRMS calcd for $C_{22}H_{36}O_3Si$ (M^+) 376.2434, found 376.2346.

Isomerization of 1e. To a suspension of **8a** (26.6 mg, 0.05 mmol) in CH_2Cl_2 solution (5 mL) were added (*E*)-**1e** (174.2 mg, 1.0 mmol) and **2a** (230.4 mg, 1.0 mmol) at −78 °C. The resulting clear solution was stirred for 2 h at this temperature. To the reaction mixture was added $NaHCO_3$, 1 N HCl, and brine. The organic layer was dried (Na_2SO_4). The mixture was filtered, and the filtrate was evaporated. GLC analysis of the crude mixture showed **5h** to be formed in 44% yield. HPLC analysis of the crude mixture showed that **1e** consisted of the *E*/*Z* isomers in a 90:10 ratio. Other reactions were carried out analogously.

Theoretical Calculations. The theoretical studies were performed at the restricted Hartree−Fock (RHF) level using the PM3 semiempirical SCF-MO method as implemented in the MOPAC program (Ver. 6.0)[17] with the MOL-GRAPH program Ver. 2.8 by Daikin Industries, Ltd. or using the *ab initio* method with Gaussian 92 program.[35] Final geometries and energetics were obtained by optimizing the total molecular energy with respect to all structural variables with no symmetry constraints and further refined by using the key word PRECISE. The transition state structures were refined by using the key word TS and checked by diagonalizing the force constant (Hessian) matrix and establishing that it had only one negative eigenvalue.[15]

Supporting Information Available: ^{1}H NMR spectra of **1**, **6d**, **6f**, **7d**, and **16** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9512968

(34) Lorberth, J.; Vahrenkamp, H. *J. Organomet. Chem*. **1968**, *11*, 111.

(35) Gaussian 92, Revision C: Frisch, M J.; Trucks, G. W.; Head-Gordon, M.; Gill, M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1992.