for the 733 observations. The molecule has a crystallographic center of inversion. The full-matrix least-squares refinement converged at $R = 0.062$ and $R_w = 0.074$. A perspective view of the structure of the diketone **7** is presented in Figure 1 and the final atomic coordinates and thermal parameters are available as supplementary material in Table I.

B. The Diperoxide 9. The supplementary material describes the procedures followed for mounting a crystal of the diperoxide **9** and collecting crystallographic data. The crystal belonged to the orthorhombic system and the data collected were consistent only with space group *Pbca* (No. 61).[20] From a total of 1686 reflections collected in a complete octant of data, 1338 were accepted as statistically above background. In the refinement described in the supplementary material 134 parameters were varied for the 1338 observations. The molecule has a crystallographic center of inversion. The full-matrix least-squares refinement converged at $R = 0.049$ and $R_w = 0.064$. A perspective view of the structure of the diperoxide **9** is presented in Figure 2 and the final atomic coordinates and thermal parameters are available as supplementary material in Table II.

Registry No. **5**, 13031-01-1; **6**, 493-03-8; **7**, 38734-05-3; **9**, 87829-76-3; **10a**, 1838-60-4; **12**, 57479-39-7; tetralin, 119-64-2.

Supplementary Material Available: Descriptions of the determination of crystal structures for the diketone **7** and the diperoxide **9**, including tables of atomic coordinates for each compound (8 pages). Ordering information is given on any masthead page.

Selective γ-Substitution of α,β-Unsaturated Esters via α-Trimethylsilyl β,γ-Unsaturated Esters

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Received May 26, 1983

In order to achieve selective γ-substitution of α,β-unsaturated esters, we investigated the directive effect of silicon in the reaction of various electrophiles with α-trimethylsilyl β,γ-unsaturated esters. These esters were prepared by nickel-catalyzed vinylation reactions of the lithium enolate of ethyl α-(trimethylsilyl)acetate. The α-silyl β,γ-unsaturated esters reacted with a variety of electrophiles (aldehydes, ketones, acetals, ketals, acid chlorides, and chloro thioethers) in the presence of Lewis acids (titanium tetrachloride and trimethylsilyl trifluoromethanesulfonate) to give exclusively the γ-substituted product in moderate to good yields. In some cases, the primary substitution products underwent additional conversions under the reaction conditions, such as the cyclization of the δ-hydroxyl or δ-keto enoates to dihydropyrones or pyrones, respectively. These α-silyl β,γ-unsaturated esters are effective reagents for achieving complete γ-selective substitution of α,β-unsaturated ester systems.

Introduction

The synthetic approach to polyisoprenoid systems that involves the direct attachment of intact isoprene units, a process termed "prenologation", is attractive in its conceptual simplicity, but in practice, it suffers from stereochemical and regiochemical ambiguities.[1] One method that has been developed to the point of considerable utility involves the selective γ-substitution of extended enolates (**2**) derived from α,β-unsaturated carbonyl compounds (**1**) (eq 1).[2-22] While the γ substituted product (**4**) displays geometric isomerism, the major task in the approach is to direct electrophilic substitution upon the enol derivative

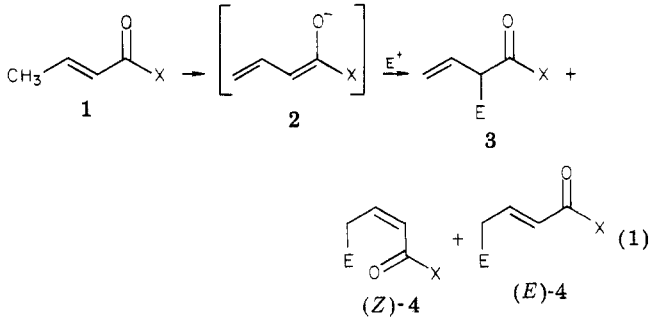

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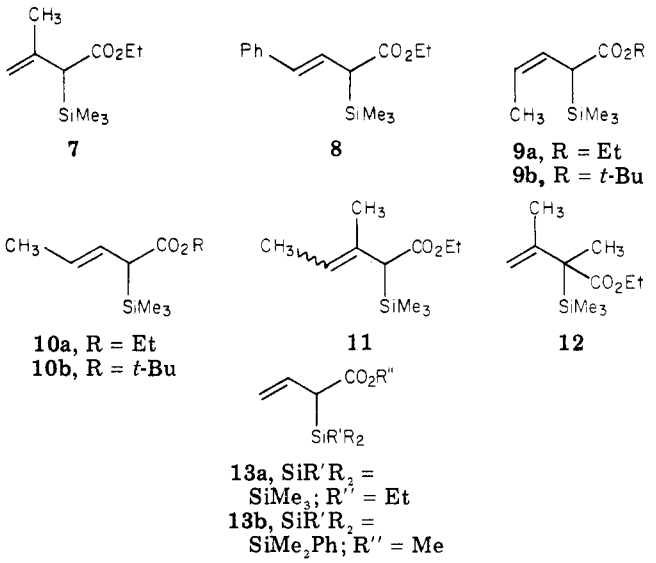
Chart I

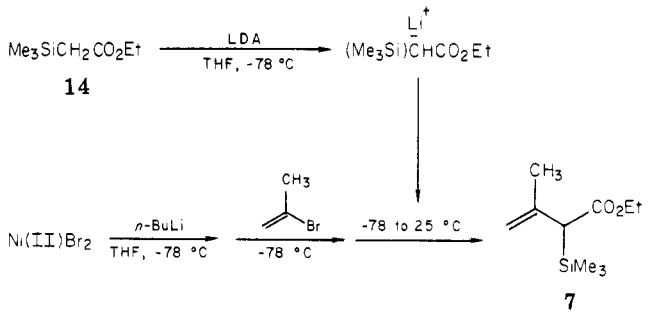


to the γ site, since such substitutions normally have strong preference for the α-carbon, giving **3**.[2,23] Factors such as the presence of a heteroatom on the β- or γ-carbon of the dienol system,[3-9] the nature of the metal counterions,[10-15,22] the solvent,[11] temperature,[11,17] and electrophile[12,16,22] have all been found to alter the α- to γ-substitution ratio.

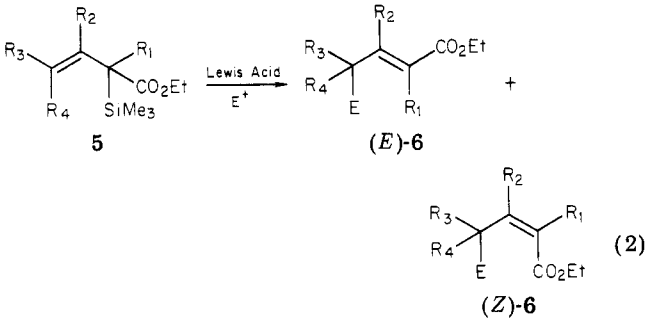
One interesting approach for enhancing the selectivity of γ-substitution of unsaturated carbonyl compounds involves the reaction of the corresponding silyl dienol ether[24-26] with electrophiles in the presence of Lewis acids. Although these reactions do exhibit enhanced γ-selectivity, the formation of α-adducts and/or geometrical isomers is not precluded.[25,26] Still, these results were suggestive of the use of silicon in controlling alkylation regioselectivity.

Silicon in an allylic silane is known to exert a strong γ-directing influence upon reactions with electrophiles,[27-29] which is presumed to be a consequence of its capacity for

Scheme I



stabilizing β-cations.[27,28,30-33] Thus, we felt that placement of a silyl group at the α-position of a β,γ-unsaturated ester might ensure that the attack of an electrophile would proceed with very high γ-selectivity. Upon reaction with an electrophile, in the presence of Lewis acids, such a system (**5**) would undergo allylic transposition to give the γ-substituted ester **6**.



In this report, we describe the preparation of α-trimethylsilyl β,γ-unsaturated esters **7–12** (see Chart I), and we demonstrate that these esters undergo clean γ-substitution in the presence of Lewis acids. In addition, high trans stereoselectivity about the 2,3-double bond is normally also observed. Subsequent to a preliminary account of a portion of this work,[34] there appeared two reports[35,36] concerning the synthesis and reactions of the ester **13**.

Results and Discussion

Preparation of α-Trimethylsilyl β,γ-Unsaturated Esters. Rathke and Millard[37] have reported that lithium ester enolates can be vinylated or arylated by allowing them to react with a vinyl or aryl halide in the presence of a nickel catalyst generated by treating nickel(II) bromide ($NiBr_2$) with *n*-butyllithium at −78 °C. The only modification required for the application of this method to the synthesis of α-silyl β,γ-unsaturated esters is the incorporation of an α-silyl group in the ester (Scheme I). Ethyl α-(trimethylsilyl)acetate (**14**) was prepared in >90% distilled yield by a modification of the literature procedure[38] using diethyl ether as solvent in a zinc-mediated coupling of ethyl α-bromoacetate with chlorotrimethylsilane

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(Me_3SiCl). Similarly, ethyl α-(diphenylmethylsilyl)-acetate[38] was obtained in 89% yield after distillation. When the lithium anion of **14** was allowed to react with 2-bromopropene in THF with the $NiBr_2$/*n*-BuLi catalyst system[37] at −78 °C, followed by warming to room temperature for 1 h, ethyl 2-(trimethylsilyl)-3-methyl-3-butenoate (**7**) was obtained in 62% yield after fractional distillation or in 74% yield after chromatography (Scheme I). Compound **7** is stable at room temperature for months; it can be handled in an open atmosphere, and it is unaffected by mild acids, unlike many allylic silanes. The preparation of **7** can be scaled up without difficulty. The best yields were obtained when at least $^1/_2$ equiv of $NiBr_2$ was used but were not necessarily improved by larger quantities. However, the quality of the $NiBr_2$ is very important: older material, which has been exposed to air more often, tended to give lower yields; the rust-colored $NiBr_2$ obtained from Aldrich not only contained magnetic particles but gave lower yields and furnished crude material of lower purity than the golden-orange-colored powder (98%) obtained from Alfa.

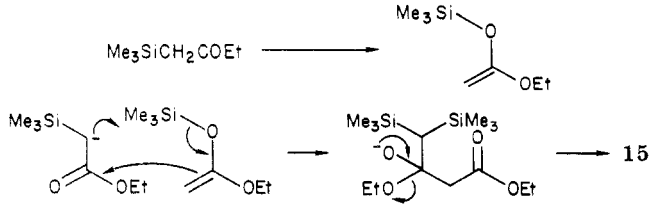
A variety of other vinylic halides were examined in the coupling reaction with mixed success; yields were generally lower and were often erratic. With β-bromostyrene, isolated yields ranged from 0% to 45%, and the α-silyl β,γ-unsaturated ester (**8**) produced is not as stable as **7**. It decomposes upon distillation, and partial protodesilylation occurs upon flash chromatography, so that the protodesilylated product often contaminates **8**.

The coupling reaction appears to operate selectively on the less hindered *E*-vinylic bromides. Thus, although the β-bromostyrene employed in the preparation of **8** was 87% trans (GLC analysis), the ester that formed is >95% *trans*-**8** with no *cis*-**8** being detected by ^1H NMR. When 98% *cis*-1-bromo-1-propene is coupled with the enolate of **14**, only an 8% yield of pure cis silyl ester **9a** is obtained. However, when a 79% cis mixture is used, a 15:8 ratio of trans (**10a**) to cis (**9a**) isomers is formed. Again, the product is greatly enriched in the trans isomer.[39] Reaction of an 80:20 isomer mixture of 2-bromo-2-butene afforded an isomeric mixture of the silyl ester **11** in yields of up to 32%.

In all of these nickel-mediated coupling reactions, a substantial amount of one byproduct was observed. Isolation and characterization showed this material to be ethyl 4,4-bis(trimethylsilyl)acetoacetate (**15**). A possible

$(Me_3Si)_2CHC(=O)CH_2CO_2Et$
15

mechanism for its formation is shown below. Rearrangement of ethyl α-(trimethylsilyl)acetate to the silyl ketene acetal, attack of the enolate upon silicon, and then condensation with loss of the ethoxy group would afford **15**.

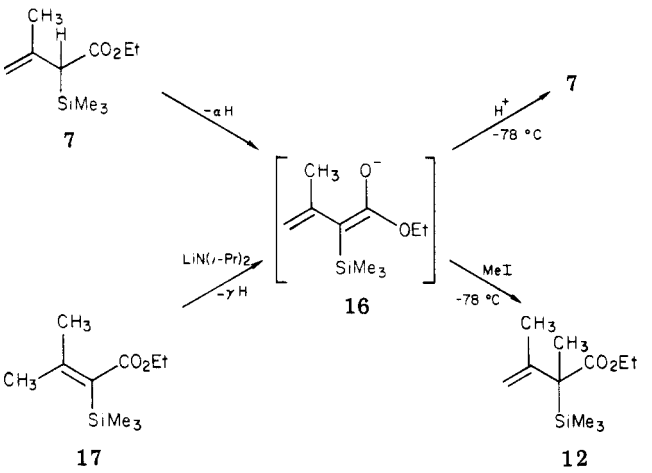


Because of the generally modest and sometimes erratic yields that we encountered in the nickel-mediated coupling approach to the α-silyl β,γ-unsaturated esters, we did make a fairly extensive examination of the effects of various solvents, reactant stoichiometries, and temperatures as well as other catalyst systems [$NiBr_2$·DME/*n*-BuLi, Ni(acac)$_2$/DIBAH, $Pd(PPh_3)_4$, $NiCl_2(PPh_3)_2$/*n*-BuLi, Fe(DBM)$_3$, CuBr·SMe_2, and photolysis] in an attempt to increase the yield of this vinylic coupling process. However, no significant improvements were achieved. We have considered a number of alternative approaches to these systems, however.

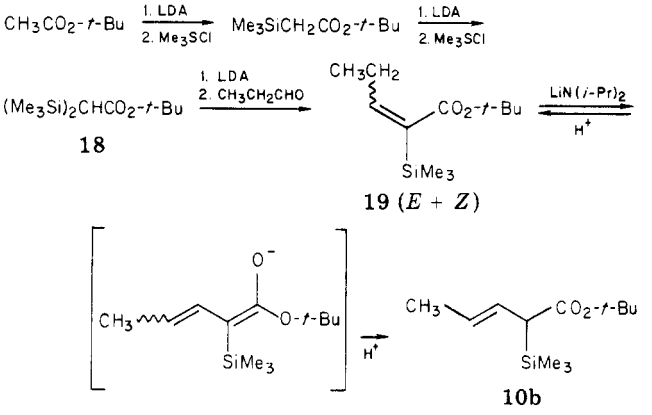
Since dienolates have a marked preference for protonation at the α-position, an α-silyl β,γ-unsaturated ester could be obtained by α-protonation of an α-silyl dienolate (see Scheme II). Since this dienolate could be generated either by α-deprotonation of the β,γ-unsaturated ester (**7**) or γ-deprotonation of the α,β-unsaturated ester (**17**), this makes the α-silyl β,γ-unsaturated esters (**17**) potential precursors of the β,γ-unsaturated isomers (**7**). The validity of this approach is indicated by the fact that when dienolate **16**, produced by treatment of **7** with LDA at −78 °C, is protonated or methylated at low temperatures, the α-substituted isomers **7** or **12** are obtained, respectively.

We have examined one route[40] to an α-trimethylsilyl

Scheme II



Scheme III



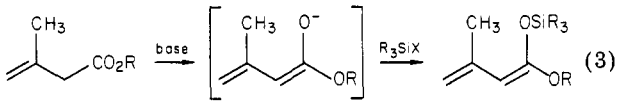
(39) There is precedent for the preferential reaction of (*E*)-vinyl halides and for *E*/*Z* isomerization of vinyl halides in nickel-catalyzed cross-coupling reactions: Sakakibara, Y.; Yadani, N.; Ibuki, I.; Sakai, M.; Ushino, N. *Chem. Lett.* **1982**, 1565, and Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jap.* **1976**, 49, 1958.

(40) Other approaches[27] to α-trimethylsilyl α,β-unsaturated esters are: formation of the vinyl anion or Grignard derived from 1-halo-1-(trimethylsilyl)-1-alkenes, followed by quenching with CO_2 and esterification; platinum-catalyzed hydrosilylation of the *tert*-butyl ester of 1-hydroxy-2-alkynes, followed by conversion of the protected hydroxyl group to the ester; treatment of 1-(trimethylsilyl)-1-alkynes with *i*-Bu_2AlH; formation of the "ate" complex with methyllithium, followed by quenching with CO_2 and esterification; nickel-catalyzed addition of a Grignard to 1-(trimethylsilyl)-1-alkynes, followed by quenching with CO_2 and esterification; and condensation of the anion derived from 2-bis(trimethylsilyl)-methyl-4,4,6-trimethyl-5,6-dihydro-1,3-oxazine with an aldehyde (to afford a masked ester).

α,β-unsaturated ester system (Scheme III).[41] The enolate derived from *tert*-butyl bis(trimethylsilyl)acetate (**18**) reacted with propionaldehyde to afford the silyl enoate **19** in 81% yield as a 1:1 isomeric mixture. Generation of the dienolate of **19** with lithium diisopropylamide (LDA) in THF at −40 °C followed by aqueous ammonium chloride workup affords a ≥2:1 mixture[42] of the desired α-silyl ester **10b** and recovered **19**. Flash chromatography affords **10b** in 75% yield, adjusted for recovery of **19**; this material is >95% trans, no *cis*-**9b** being detected by ^{1}H NMR. The temperature of dienolate generation is important, as the rate of deprotonation is very slow at −78 °C, but self-condensation begins at temperatures greater than −40 °C.

Unfortunately, it was found that the *tert*-butyl ester in **10b** is cleaved[43] in the presence of titanium tetrachloride ($TiCl_4$) or trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf) in the Lewis-acid-mediated reactions of **10b** with electrophiles, leading to complex product mixtures. Perhaps, though, another bulky ester that is less susceptible to cleavage by Lewis acids could be employed.

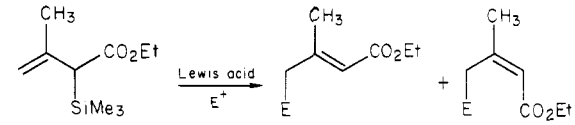
We also examined in considerable detail the conceptually most direct approach to α-silyl β,γ-unsaturated esters, viz, silylation of dienolates (eq 3). However, it was our uni-



(3)

form experience that attempts to silylate these dienolates (as their lithium, magnesium bromide, and zinc bromide salts of the acid and the ethyl or *tert*-butyl esters) in a variety of solvents (THF, ether, and THF/HMPA) with "hard" (trimethylsilyl chloride) as well as "soft" (methyldiphenylsilyl chloride)[44,45] silylating agents, led almost exclusively to the silyl dienol ether.[46]

Electrophilic Substitution of α-Silyl β,γ-Unsaturated Esters. To examine the scope and limitations of electrophilic substitution of α-silyl β,γ-unsaturated esters, the ester **7** was allowed to react with a variety of electrophiles in the presence of $TiCl_4$ or Me_3SiOTf (eq 4). The



7 (*E*)-20 (*Z*)-20 (4)

results are summarized in Tables I–III. γ-Selective reaction of **7** was observed with aldehydes and ketones (Table I, entries 1–3 and 6), acid chlorides (Table I, entries 4 and 5), ketals and acetals (Table II, entries 1–3), and chloromethyl phenyl sulfide (Table III, entry 1). The ester **7** appears to have moderate reactivity; so, reactions proceed at reasonable rates between −78 °C and room temperature. Products could be isolated conveniently by preparative thin-layer chromatography. In all cases, *only products resulting from attack of the electrophile on the γ-carbon* ((*E*)-**20** and (*Z*)-**20**) *were observed; no α-substituted products could be detected* by GLC or ^{1}H NMR. Chloromethyl phenyl sulfide (**46**), an electrophile known to give low γ:α ratios when reacted with silyl dienol ethers,[25] also gives clean γ-selectivity with ester **7**, albeit with lower stereoselectivity (*E*:*Z* ca. 1:1) than is observed in most cases (*E*:*Z* ca. 9:1).

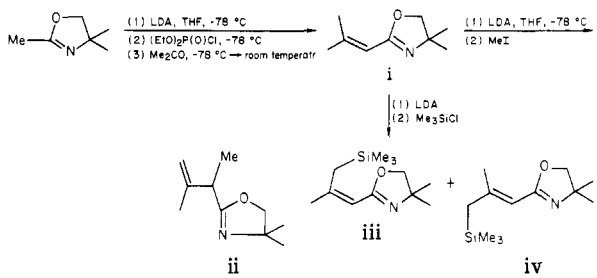
Products arising from the reaction of **7** with acid chlorides or aldehydes and ketones (the δ-keto or δ-hydroxy esters) were often found partially cyclized to the α-pyrones (Table I, entries 4 and 5) or the dihydro-α-pyrones (Table I, entries 1 and 6, and Table II, entries 4 and 5), respectively. The products isolated from the reactions of **7** with aldehydes, ketones, and acetals promoted by $TiCl_4$, TiF_4, or $FeCl_3$ appeared, in some cases, to arise from subsequent conversion of the initially formed products [chlorination (Table I, entry 6), bis substitution (Table I, entry 2, and Table III, entry 7), and dimerization (Table II, entry 6)]. Reactions of **7** with electrophiles promoted by $BF_3{\cdot}OEt_2$ afforded complex product mixtures. In contrast, these further transformations were not observed with acetals and Me_3SiOTf as catalyst.

Reactions employing other α-silyl β,γ-unsaturated esters (**8**, **9**, **11**, and **12**) were then investigated (Table III). The esters **9** and **11** were similar to **7** in terms of relative reactivity, stereo- and regioselectivity, and further reactivity of the primary adducts. The ester **12** is less reactive than **7**.

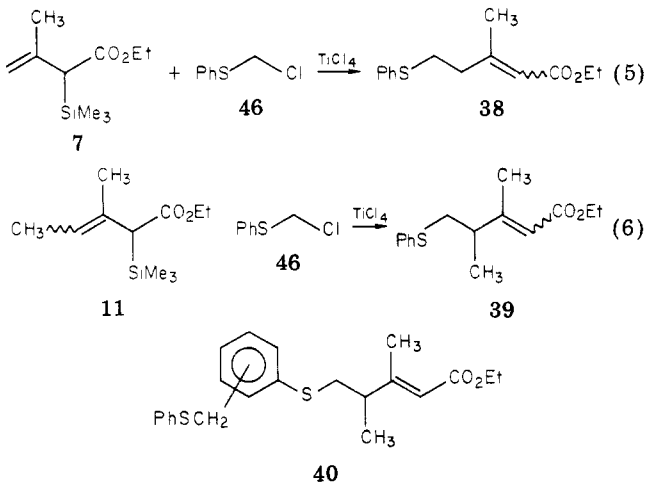
γ-Regioselectivity. In all reactions of the α-silyl β,γ-unsaturated esters with electrophiles promoted by Lewis acids, complete γ-regioselectivity was observed; no α-substituted adducts could be detected by GLC or ^{1}H NMR. The most interesting way to examine the limit of γ-regioselectivity of our α-silyl β,γ-unsaturated ester system is to compare it with the system that shows the next most γ-selective electrophilic substitution, the silyl dienol ether system described by Fleming.[25] In Fleming's system, many electrophiles reacted with good γ-regioselectivity; chloromethyl phenyl sulfide (**46**), however, gave a low γ- to α-substitution ratio. In contrast, the $TiCl_4$ promoted reaction of **7** with **46** afforded only the isomeric γ-substituted adducts **38** in 52% yield after chromatography (eq 5). GLC and ^{1}H NMR analysis of the crude reaction mixture indicated only the presence of the γ-adducts (as a 44:56 mixture of *E*:*Z* isomers); no α-adduct was detected.

Likewise, the $TiCl_4$-promoted reaction of **11** with **46** afforded no α-adducts (eq 6). However, in addition to the desired adduct **39**, obtained in a 20% yield, the doubly substituted product **40** was also obtained, in a 12% yield, as well as some protodesilylated material. Whether the (phenylthio)methylation that leads to **40** occurred upon another molecule of chloromethyl phenyl sulfide, followed

(41) Hartzell, S. L.; Rathke, M. W. *Tetrahedron Lett.* **1976**, 2737.
(42) This ratio was obtained from a small scale reaction and may not represent the optimum value.
(43) See Reference 25b and Greene, T. W. "Protective Groups in Organic Synthesis"; Wiley: New York, 1981.
(44) Larson, G. L.; Fuentes, L. M. *J. Am. Chem. Soc.* **1981**, *103*, 2418.
(45) Larson and Fuentes[44] reported that C-substitution occurs predominantly in the reaction of several ester enolates with $Ph_2MeSiCl$. However, we found that the dienolate of ethyl crotonate failed to undergo any silylation when treated with $Ph_2MeSiCl$ under various conditions, an observation also confirmed by Larson (private communication).
(46) Attempts to achieve a direct α-silylation of masked sources of unsaturated carbonyl compounds, such as nitrile[47] and oxazoline, were also unsuccessful. The dienolate of the oxazoline i, synthesized via



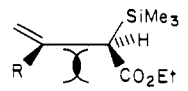
Meyer's method,[48] afforded the α-substituted adduct ii when reacted with methyl iodide but afforded predominantly the γ-substituted adducts iii and iv when reacted with chlorotrimethylsilane under various conditions. This behavior is analogous to that of lithiated unsaturated imines.[18,20,49]
(47) (a) Brenner, S.; Bovete, M. *Tetrahedron Lett.* **1974**, 1377. (b) Watt, D. S. *Synth. Commun.* **1974**, *4*, 127.
(48) Meyers, A. I. *Acc. Chem. Res.* **1978**, *11*, 375.
(49) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, 7.



by reaction with **11**, or upon the adduct **39** is unknown. In contrast to the aforementioned reaction with **7** in which no stereoselectivity was seen, the diadduct **40** is obtained predominantly as the trans isomer. The diadduct **40** was also separable into two components differing in aryl substitution pattern, but the site of substitution could not be assigned.

Relative Reactivity of α-Silyl β,γ-Unsaturated Esters. Compared to that of other allylsilanes, the nucleophilic reactivity of α-silyl β,γ-unsaturated esters is relatively low. Even with warming to room temperature, complete consumption of these esters often takes upwards of 15 h (for example, see Tables I, II, and III). Further evidence of reduced nucleophilicity is the failure of **7** to react with a number of electrophiles: allyl bromide, dimethylallyl chloride, phenyl chloroformate, and 1-(4-methoxyphenyl)-1-methoxypropane with $TiCl_4$ promotion; allyl–palladium complexes of allyl bromide or geranyl acetate with $Pd(PPh_3)_4$ catalysis;[50] triethyloxonium tetrafluroborate as both electrophile and promoter; and hexanal with tetra-*n*-butylammonium fluoride as promoter.[51] Complex product mixtures were obtained from the $TiCl_4$-promoted reactions of **7** with methacrolein, butadiene monoxide, and cyclohexenone. Separation of the latter product mixture afforded predominantly polymers of cyclohexenone and a minor amount of a mixture of the adducts resulting from 1,2- and 1,4-addition to cyclohexenone.

In studying a related system (**13a**), Oshima and coworkers[35] found that **13a** also would not react with primary or benzylic halides. However, it did react in an S_N2 manner with allylic ethers and halides in which the leaving group was on a secondary carbon. Surprisingly, the ester **13a** was found not to be sluggish in reactivity when it did react, the reactions being over in less than an hour at −78 °C. This implies that the sluggish reactivity of the α-silyl β,γ-unsaturated esters studied in this report, e.g., **7**, may

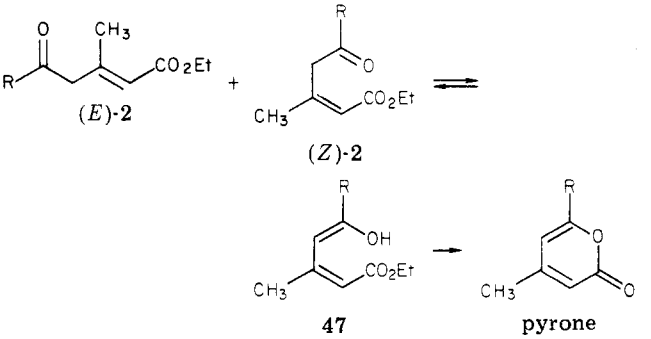


7, R = CH_3
13a, R = H

(50) In contrast, allylstannanes do couple with allylic acetates or allylic halides, catalyzed by palladium(0): (a) Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599. (b) Trost, B. M.; Keinan, E. *Ibid.* **1980**, *21*, 2595.

(51) Failure may be due to traces of moisture that are difficult to remove from the salt. See: (a) Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 1025. (b) Andersen, N. H.; McCrae, D. A.; Grotjahn, D. B.; Gabhe, S. Y.; Theodore, L. J.; Ippolito, R. M.; Sarkar, T. K. *Tetrahedron* **1981**, *37*, 4069.

Scheme IV



be due to steric effects rather than electronic effects. By this we mean the presence of the methyl substituent at the β carbon as in **7** (see R in the structure) may interfere with the attainment of the perpendicular arrangement of the carbon–silicon bond with the double bond needed to activate the system toward the attack by electrophiles. This steric impediment is not present in **13a**.

Further support of the role of steric factors in retarding the reactivity was the behavior of the very hindered ester **12**; when Me_3SiOTf was used as catalyst, **12** failed to react with the dimethyl acetal of acetone, affording instead a 91% yield of the protodesilylated ester after workup. Reaction of **12** with trimethylacetyl chloride in the presence of $TiCl_4$ did provide a 3:1 mixture of the δ-keto esters and the α-pyrone (Table III, entry 3), albeit in 36% yield.

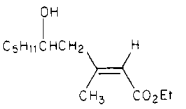
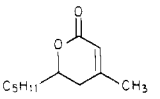
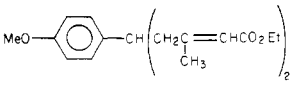
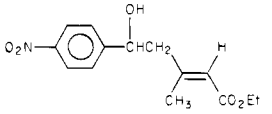
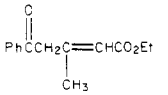
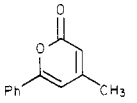
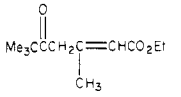
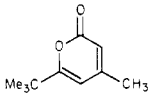
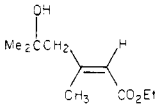
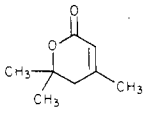
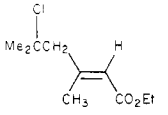
Further Reaction of Primary Products. The primary products from the Lewis-acid-mediated reactions of α-silyl β,γ-unsaturated esters with various electrophiles often underwent further transformations. Cyclization to α-pyrones and α-dihydropyrones occurred from the cis δ-keto and cis δ-hydroxy esters obtained from the reactions with acid chlorides and aldehydes or ketones, respectively. The α-pyrone presumably arises via the dienol **47** (Scheme IV). This is supported by the fact that the α-pyrone becomes the predominant product when the enol form is well stabilized by an aryl substituent (Table I, entry 4). The crude mixture of δ-keto esters could also be cleanly converted to the α-pyrone in high yield by treatment with a catalytic amount of sodium ethoxide in ethanol. For example, the reaction of **7** with trimethylacetyl chloride was repeated to yield a product mixture predominant in the δ-keto esters, **27**. The crude products were treated with 10 mol % of sodium ethoxide in ethanol at room temperature to afford 4-methyl-6-*tert*-butyl-2*H*-2-pyrone (**28**) in ≥74% yield from **7** after purification.

From the reaction of **7** with hexanal (Table I, entry 1), the cis isomer also was isolated as the α-dihydropyrone. However, a low product yield was realized because of excessive product loss which occurred upon chromatography, partially from elimination to the diene. No attempts were made to maximize the yield. A low yield of adducts was also realized from the reaction of **9** with propionaldehyde in the presence of $TiCl_4$.

The reaction of **7** with acetone (Table I, entry 6) afforded not only the trans isomer (**29**) and the dihydropyrone (**30**), resulting from cyclization of the cis isomer, but a trans chloro adduct (**31**) as well. Although the isolation of such an adduct has not been described in the $TiCl_4$-promoted reactions of allylsilanes with electrophiles, there are reports that chloro adducts have been isolated from the $TiCl_4$-promoted reaction of propynylsilanes with carbonyl compounds[52] and from Friedel–Crafts acylations of olefins[53]

(52) Pornet, J.; Randrianoelina, B. *Tetrahedron Lett.* **1981**, *22*, 1327.

Table I. Reaction of 7 with Carbonyl Compounds in the Presence of $TiCl_4$[a]

entry	electrophile	temp, °C, time		products (ratio)[b]	yield, % (crude, purified)[c]
1	$C_5H_{11}CHO$	−78, 12 h, −30, 3 h	21	 (92)	86, 22[d]
			22	 (8)	
2	*p*-$MeOC_6H_4CHO$	−78, 24 h	23	 ($E,E:E,Z$ = 82:18)	72, *e*
3	*p*-$O_2NC_6H_4CHO$	−78, 16 h	24	 (E = >95)[f]	89, 65
4	PhCOCl	room temp, 33 h	25	 (28)[g]	~100, 49
			26	 (72)	
5	Me_3CCOCl	room temp, 23 h	27	 (82)[g]	86, 58
			28	 (18)	
6	$(CH_3)_2CO$	room temp, 24 h	29	 (76)	71, *e*
			30	 (10)	
			31	 (14)	

[a] In a typical procedure 1.1 equiv of an electrophile is added to a solution of $TiCl_4$ (0.181 mL, 1.65 mmol, 1.1 equiv) in 2 mL of CH_2Cl_2 at −78 °C, followed by a solution of 7 (301 mg, 1.5 mmol, 1.0 equiv) in 2 mL of CH_2Cl_2. The reaction was stirred at −78 °C for 15 min and then stirred under the conditions stated in the table. [b] Determined by GLC before purification. [c] Sum of yields of all components after isolation by chromatography. [d] No attempt was made to maximize yield. [e] Not determined. [f] Only one isomer detected by ^1H NMR. [g] Mixture of isomers contained a nonseparable, unidentified component.

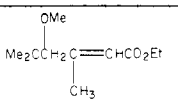
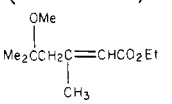
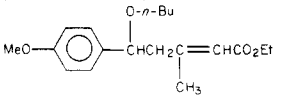
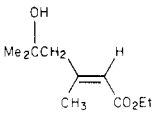
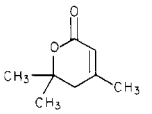
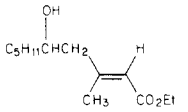
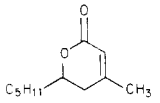
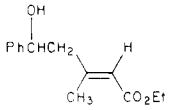
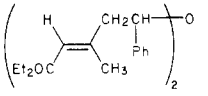
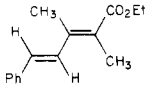
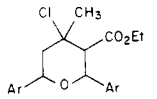
and vinylsilanes[54] with acid chlorides in the presence of a chlorinated Lewis acid.

The $TiCl_4$-promoted reaction of **11**, predominantly as the trans isomer (i.e., *cis*-methyls), with benzaldehyde (Table III, entry 4) afforded, after purification, a 44% yield of diastereomeric chloroadducts **43** along with a 21% yield of a component identified as an isomeric mixture of *E* and *Z* ethyl 2-acetylcinnamate (**44**). Comparison with authentic **44** synthesized by Knoevenagel condensation of ethyl acetoacetate with benzaldehyde, supported the identification. A possible explanation for the occurrence of **44** is outlined in Scheme V. The intermediacy of zwitterion **48** seems plausible for the carbonium ion is well stabilized, being both tertiary and β to the silyl group. Appropriate alignment of silicon with the p orbital and subsequent elimination of the silyl group would give the alkoxy adduct **49**, which leads to the major product **43**. If proper alignment for elimination was sterically hindered or was slow to be reached in comparison to intramolecular attack by the alkoxy group, then ring closure would afford an oxetane **50**.[55] Lewis-acid-assisted cleavage[56] of **50**, but

(53) Hacini, S.; Pardo, R.; Santelli, M. *Tetrahedron Lett.* **1979**, 4553.
(54) (a) Fristad, W. E.; Dime, D. S.; Bailey, T. R.; Paquette, L. A. *Tetrahedron Lett.* **1979**, 1999. (b) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *J. Org. Chem.* **1980**, *45*, 3017.

(55) 2-Silyalkyloxetanes, arising from the intramolecular attack of a hydroxyl group upon silyl-stabilized carbocation, have been described by Ehlinger, E.; Magnus, P. D. *J. Chem. Soc., Chem. Commun.* **1979**, 421.

Table II. Reaction of 7 with Electrophiles Promoted by Various Lewis Acids[a]

entry	electrophile	Lewis acid	temp, °C, time		products (ratio)		yield, % (crude, purified)[b]
1	$Me_2C(OMe)_2$	$TiCl_4$	−78, 22 h, 0, 9 h	32	 ($E:Z$ = 91:9)[c]		~100,[d] e
2	$Me_2C(OMe)_2$	Me_3SiOTf	−78, 26 h	32	 ($E:Z$ = 86:14)[c]		~100, 83
3	p-$MeOC_6H_4CH(O$-n-$Bu)_2$	Me_3SiOTf	−78, 2 h	33	 ($E:Z$ = 97:3)[c]		~100, 81
4	$(CH_3)_2CO$	TiF_4	−32, 5 h, 0, 5 h, room temp, 15.5 h	29			16, c
				30			
5	$C_5H_{11}CHO$	TiF_4	−78, 5 h, room temp, 22 h	21		(84)[f]	88, 31[g]
				22		(16)[f]	
6	PhCHO	TiF_4	−78, 90 min, −32, 90 min, room temp, 7 h	34		(19)[f]	~100, 83
				35		(77)[f]	
				36		(4)[f]	
7	p-$O_2NC_6H_4CHO$	$FeCl_3$	−78, 4 h, room temp, 13.5 h	37			~100, 86[h]

[a] For a typical reaction see footnote *a* of Table I, with $TiCl_4$, Me_3SiOTf (17 mg, 0.05 equiv), or TiF_4,(204 mg, 1.1 equiv) as promoter. [b] Sum of yields of all components after isolation by chromatography. [c] Determined by GLC before purification. [d] Crude material contained starting material and other unidentifiable components. [e] Not determined. [f] Ratio of isolated yields. [g] Another major component was isolated but could not be identified. [h] Mixture of diastereomers.

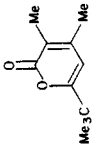
with scission at b, would then afford the zwitterion **51**, further cleavage of which affords β-methylstyrene and ethyl 2-(trimethylsilyl)acetoacetate (**52**). Knoevenagel-type Peterson condensation of **52** with benzaldehyde, catalyzed by $TiCl_4$,[57] gives **44**.

The reaction of **7** with *p*-nitrobenzaldehyde in the presence of ferric chloride ($FeCl_3$)[58] (Table II, entry 7) gave tetrahydropyran **37** in 86% yield (based on *p*-nitrobenzaldehyde) as a mixture of diastereomers. Although, as in the case of the processes shown in Scheme V, one can formulate a reaction path that involves an oxetane, a more plausible mechanism for the formation of **37** is outlined in Scheme VI. The weaker iron–oxygen interaction (Fe–O bond 96 kcal/mol compared to 158 kcal/mol for Ti–O bond)[59] may be important in the formation of the hemiacetal intermediate whose ionization preceeds cyclization to the tetrahydropyran cation and chloride in trapping. Treatment of **37** with DBU effected, albeit in low yield, dehydrochlorination to give the dihydropyran **53**.

The formation of halogenated byproducts could be eliminated by the use of titanium tetrafluoride as promoter. With acetone or hexanal as the electrophile (Table

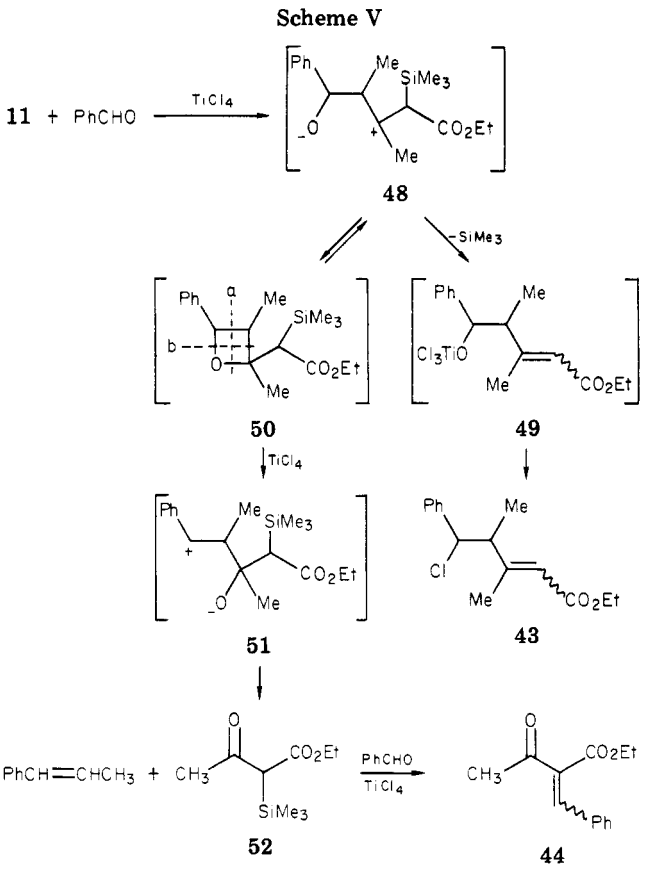
(56) Jones, G., II in "Organic Photochemistry"; Padwa, A., Ed., Marcel Dekker: New York, 1981; Vol. 5.
(57) (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780. (b) Jones, G. *Org. React.* (N.Y.) **1967**, *15*, 267.
(58) Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642.
(59) "CRC Handbook of Chemistry and Physics", 54th ed.; Weast, R. C., Ed.; CRC Press: Cleveland, OH, 1973; p F-200.

Table III. Electrophilic Substitution of Various α-Silyl β,γ-Unsaturated Esters[a]

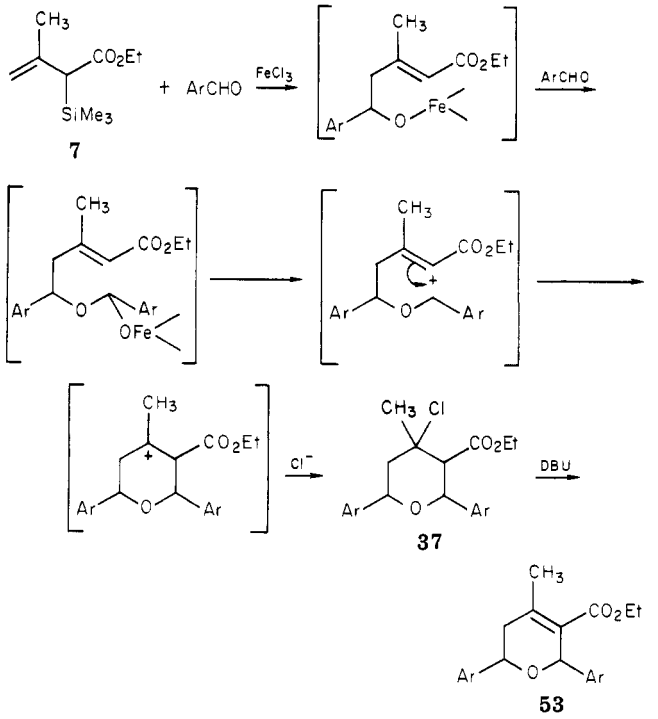
entry	α-silyl ester	electrophile	Lewis acid	temp, °C, time		products (ratio)	purified yield, %
1	7	$PhSCH_2Cl$	$TiCl_4$	0, 24 h	38	$PhSCH_2CH_2C(CH_3)=CHCO_2Et$ ($E:Z$ = 44:56)	52[b]
2	11	$PhSCH_2Cl$	$TiCl_4$	0, 10 h, room temp, 11 h	39	$PhSCH_2CH(CH_3)C(CH_3)=CHCO_2Et$ ($E:Z$ = 54:46)	20[b]
					40	$PhSCH_2C_6H_4SCH_2CH(CH_3)C(CH_3)=CHCO_2Et$ (high R_f $E:Z$ = 89:11) (low R_f $E:Z$ = 80:20)	12
3	12	Me_3CCOCl	$TiCl_4$	−78, 8 h, room temp, 40 h	41	$Me_3CCOCH_2C(CH_3)=C(CH_3)CO_2Et$	26[b]
					42		10
4	11	PhCHO	$TiCl_4$	−78, 8 h, room temp, 21 h	43	$PhCH(Cl)CH(CH_3)C(CH_3)=CHCO_2Et$	44
					44	$PhCH=C(COCH_3)CO_2Et$	21
5	8	p-$MeOC_6H_4CH(O$-n-$Bu)_2$	Me_3SiOTf	−78, 4.5 h, room temp, 17 h	45	p-$MeOC_6H_4CH(n$-$BuO)CH(Ph)CH=CHCO_2Et$[c]	60[d]

[a] For a typical procedure, see footnote *a* of Table I, with $TiCl_4$, Me_3SiOTf (17 mg, 0.05 equiv), or TiF_4 (204 mg, 1.1 equiv) as promoter and the appropriate ester instead of 7. [b] Crude material contains some protodesilylated ester. [c] See text for tentative stereochemical assignments. [d] A 20% yield of protodesilylated ester was also obtained.

Scheme V



Scheme VI[a]

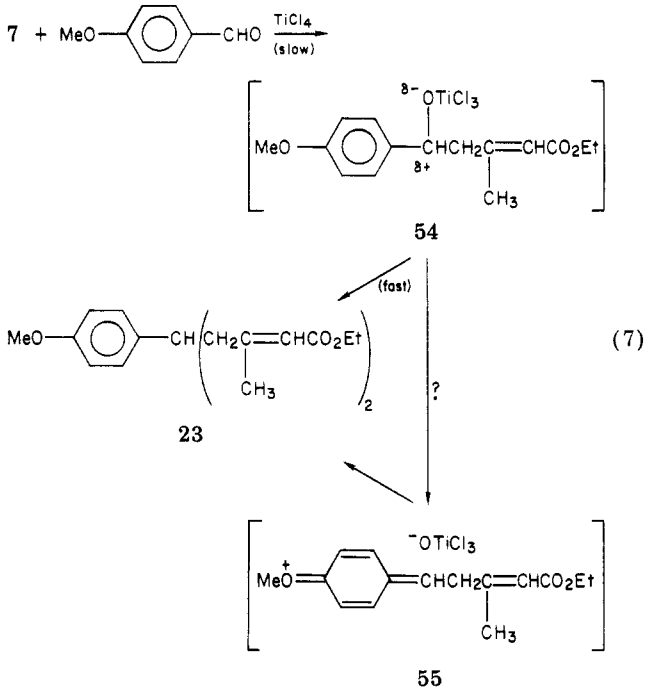


[a] Ar = p-$NO_2C_6H_4$.

II, entries 4 and 5) the trans adducts and the α-dihydropyrones were obtained, albeit in relatively low yields, without formation of halogen-containing byproducts. In the case of hexanal, the major product appears to be a dimeric species that was not fully characterized but may be analogous to the major ether dimer produced in the reaction with benzaldehyde (Table II, entry 6). This ether (**35**) is formed, along with the diene **36**, when the mono-

adduct **34** is treated with titanium tetrafluoride.

Another noteworthy side reaction is that of **7** with *p*-anisaldehyde (Table I, entry 2) in which dialkylated products **23** were obtained. Evidently the intermediate adduct **54**, or the resonance-stabilized adduct **55**, is more activated toward nucleophilic attack than is further reaction with $TiCl_4$ activated *p*-anisaldehyde (eq 7). In



(7)

contrast, the reaction with *p*-nitrobenzaldehyde (Table I, entry 3) afforded the monoadduct in high yield.

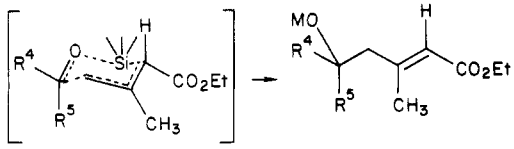
Geometric Stereoselectivity. It is noteworthy in the reactions of **7** with electrophiles that a relatively consistent ratio of trans:cis isomers about the α,β double bond in the alkylated products is observed. The average ratio (excluding the enolizable δ-keto esters from the reaction with acid chlorides and excluding the reaction with chloromethyl phenyl sulfide) is 92:8, trans:cis. This ratio is even manifested in the dialkylated products **23** from the reaction with *p*-anisaldehyde (Table I, entry 2). In this case, a ratio of 90:10 fits the quadratic formula $(a + b)^2$, i.e.,

$$(a + b)^2 = a^2 + 2ab + b^2$$

$$(0.9E + 0.1Z)^2 = 0.81E,E + 0.18E,Z + 0.01Z,Z$$

The observed ratio was 82% *E,E* and 18% *E,Z*. The only deviations are the reaction of **7** with *p*-nitrobenzaldehyde, which afforded the monoadduct with >95% stereoselectivity, and the reaction of **7** with benzaldehyde, which afforded only the *trans*-hydroxy adduct **34**, the trans dimeric ether **35**, and the 2*E* diene **36**. Oshima and coworkers[35] do not report the formation of cis isomers in the allylic couplings of **13a**.

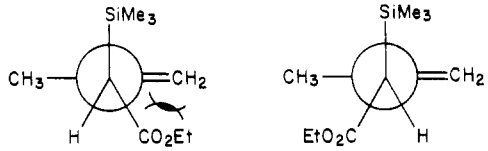
The predominance of the trans geometry in the products derived from **7** can be rationalized equally well on the basis of a cyclic transition state (**56**), where the trans isomer predominates because the carbethoxy group prefers to adopt a pseudoequatorial position (eq 8), or on the basis



56

(8)

of an open-chain transition state, where reaction via conformer **57b** is preferred because it avoids the eclipsing-type interaction encountered in **57a**. Although we have not

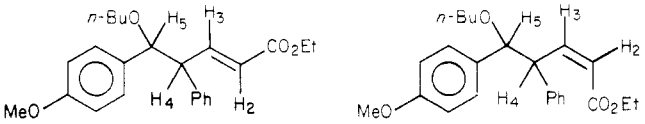


57a (gives 2-cis product) **57b** (gives 2-trans product)

come to any definitive conclusion about whether this reaction proceeds via a cyclic or an acyclic transition state (see below), it is of note that the reaction of **7** with phenyl chloromethyl sulfide, where a cyclic transition state is precluded, is the only one that shows no trans stereoselectivity.

Nature of the Transition State. Recently, many investigators have sought to elucidate the stereochemistry of the reaction of allylic silanes with electrophiles, addressing in particular the questions of whether the S_E' reaction proceeds in a syn or anti fashion and whether cyclic or open chain transition states are involved.[60,61] Recently, an antiperiplanar acyclic transition state has been proposed to account for observed erythro selectivity in the reaction of allylic silanes with carbonyl compounds.[60] However, at this point it is not at all certain that a single mechanism will be universally applicable in all systems, since the electronic influence of silicon appears to be a relatively modest one,[33,62] and the stereochemical course of a particular coupling reaction thus may be influenced strongly by the steric and electronic effect of the other substituents on the allylic silane and electrophile components.

We have attempted to examine the nature of the transition state of the reaction of the α-silyl esters with carbonyl compounds, specifically with respect to its cyclic or open-chain nature, by studying the reactions of the esters **8–11** with various electrophiles; the γ-substituent on these esters provides a potential probe of the reaction diastereoselectivity. Unfortunately, the reaction of **9** with propionaldehyde afforded adducts in only low yield, and the reaction of **11** with benzaldehyde afforded chloroadducts in which the stereochemistry at the benzylic center could have been compromised by an S_N1 or miltiple S_N2 displacements. However, reaction of **8** with the di-*n*-butyl acetal of *p*-anisaldehyde using Me_3SiOTf as catalyst afforded a 60% yield of diastereomeric adducts **45** (along with a 20% yield of protodesilylated material (eq 9)).



45a **45b**

Purification by preparative thin-layer chromatography, followed by separation on a 5-μm silica gel HPLC column, afforded the two diastereomers in an average ratio of 65:35, the major diastereomer eluting first. A very minor third

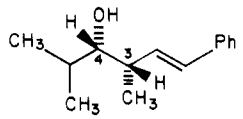
(60) (a) Hayashi, T.; Ito, H.; Kumada, M. *Tetrahedron Lett.* **1982**, *23*, 4605. (b) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (c) Hayashi, T.; Konishi, M.; Kumada, M. *Ibid.* **1982**, *104*, 4963. (d) Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281.

(61) (a) Wickham, G.; Kitching, W. *J. Org. Chem.* **1983**, *48*, 612. (b) Young, D.; Kitching, W. *Ibid.* **1983**, *48*, 614.

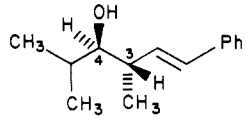
(62) Mikami, K.; Kishi, N.; Nakai, T. *Tetrahedron Lett.* **1983**, *24*, 795.

component eluted last, but not enough could be isolated for identification.

We have been unable to make complete, definitive assignments of the stereochemistry of these products. It is clear from the magnitude of the olefinic coupling that **45a** has the 2*E* geometry ($J_{2,3}$ = 16 Hz) and **45b** the 2*Z* geometry ($J_{2,3}$ = 4 Hz). However, both isomers show large vicinal coupling between the hydrogens on C-4 and C-5 (**45a**, $J_{4,5}$ = 10 Hz; **45b**, $J_{4,5}$ = 7.5 Hz). Based on the behavior of β-hydroxy carbonyl compounds, where $J_{threo} > J_{erythro}$ (J_{threo} typical 7–10 Hz),[63] one might be tempted to assign both isomers as threo. However, this NMR based stereochemical assignment system was developed with β-hydroxy ketones, in which conformational mobility is restricted by intramolecular hydrogen bonding, and thus, is not an adequate precedent for making assignments in these more mobile homoallylic alcohol systems. In fact, in some more closely related systems (**58a** and **58b**) the



58a ($J_{3,4}$ = 7 Hz)



58b ($J_{3,4}$ = 7 Hz)

vicinal couplings of both erythro and threo diastereomers are the same.[64] Without more definitive assignment of the relative stereochemistry of these reaction products, it is not possible to speculate further about the nature of the transition state of the reaction.

Conclusions

α-Silyl β,γ-unsaturated esters are useful reagents for achieving a new conversion that represents a highly regioselective γ-substitution upon α,β-unsaturated ester systems. A number of the α-silyl β,γ-unsaturated esters have been prepared by vinylic coupling processes, and their reaction with a variety of electrophiles has been exemplified. All of these have been consistently illustrative of the powerful regiodirective effect of the silicon. However, the preparation of the silyl ester systems has not always been efficient and straightforward, and because of the relatively low nucleophilicity of these systems, their reaction is restricted to that with highly electrophilic species; in particular, they fail to react with alkylating agents other than chloro thioethers; side reactions and additional conversions are also observed. Nevertheless, these reagents provide an efficient access into many interesting γ-substituted enoate systems, as well as into pyrones and dihydropyrones, and they represent an interesting use of the α-silyl group to achieve complete regiochemical control over a substitution process that is generally considered nonregioselective.

Experimental Section

Analytical gas–liquid phase chromatography (GLC) was performed on a Hewlett-Packard 5750 instrument equipped with a flame ionization detector, using a nitrogen carrier gas flow. Columns used were a 6 ft, 8 ft, or 14 ft × 0.125 in. 3% OV-17 on 100/120 Supelcoport and a 6 ft × 0.125 in., 3% Carbowax 20 M on 80/100 Gas Chrom Q. Preparative GLC was performed on a Varian Aerograph gas chromatograph, Model 90-P3, with a thermal conductivity detector, using a helium carrier gas flow and a 12 ft × 0.25 in., 3% OV-17 on 80/100 Supelcoport column.

Thin-layer chromatography was performed on 0.2-mm silica gel, glass-backed plates with F-254 indicator (Merck). Visualization was by ultraviolet light or iodine. Preparative thin layer chromatography was performed on 2-mm silica gel, glass-backed plates with F-254 indicator (Merck) or 2-mm phosphate buffered silica gel, glass-backed plates prepared by using 300 g of silica gel (Macherey, Nagel and Co. P/UV_{254}), 540 mL of water, and 60 mL of 1 M phosphate buffer, pH 7 (KH_2PO_4/Na_2HPO_4). Flash chromatography was performed with a 6-in. silica bed [32–63 micron particle size (Woelm)] in a glass column of diameter as recommended by Still.[65]

Proton magnetic resonance spectra were recorded on a Varian EM-390, a Varian HR-220, or a Nicolet NT-360 spectrometer. The chemical shifts are expressed in parts per million downfield from tetramethylsilane internal standard except for compounds containing a trimethylsilyl group, in which chloroform or methylene chloride were used as an internal standard. ^1H NMR data are presented in the form: δ value (multiplicity, coupling constants (if any, in Herz), number of protons). Infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer or Nicolet 7199C Fourier Transform spectrophotometer and are expressed as units of frequency (cm^{-1}). Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Melting points and boiling points stated are uncorrected.

Elemental analyses were performed by the University of Illinois Microanalytical Laboratory. Mass spectra were recorded on a Varian-MAT CH-5 spectrometer. High-resolution mass spectra (HRMS) and field-desorption mass spectra were recorded on a Varian MAT-731 (or 311A). Data are presented in the form: *m/z* (intensity relative to base peak).

Tetrahydrofuran (THF) was distilled from sodium–benzophenone ketyl. All other solvents were dried and stored over 3 Å molecular sieves. Diisopropylamine was distilled from calcium hydride and stored under dry nitrogen. *n*-Butyllithium was titrated periodically with 2,5-dimethoxybenzyl alcohol as indicator.[66] Titanium tetrachloride was distilled and stored under dry nitrogen. Most commercially supplied chemicals were distilled and stored over molecular sieves prior to use. Zinc metal (granular, 20 mesh) was washed prior to use (4.5 g of zinc on a sintered glass funnel was washed with 50 mL of 5% HCl, 50 mL (2 ×) of water, 50 mL of ethanol, and 50 mL of diethyl ether) and then dried under vacuum.

All reactions involving moisture sensitive compounds were performed in glassware dried for a minimum of 2 h at 120 °C. Such reactions were run under a positive pressure atmosphere of nitrogen or argon, predried by use of a Drierite drying tower. Transfer of moisture-sensitive liquids was performed by hypodermic syringe via a rubber septum on the sidearm of the reaction flash or, especially in the case of titanium tetrachloride, via a Teflon stopcock.

Ethyl α-(Trimethylsilyl)acetate (14). This ester was prepared by a slight modification of the procedure of Fessenden and Fessenden[38] using ether in place of ether–benzene. In this way we were able to obtain ester **14** in 91% yield as a colorless oil after distillation, bp 72–74 °C (~47 mm).[67] ^1H NMR spectrum matched that in the literature.[38] Mass spectrum (70 eV) *m/z* (%) no M^+, 145 (23.4), 117 (33), 115 (34.7), 103 (88.3), 75 (99), 73 (100).

Anal.[69] Calcd for $C_7H_{16}O_2Si$: C, 52.45; H, 10.06. Found: C, 52.68; H, 9.89.

(63) The terms erythro and threo are used in the convention defined by Heathcock[63a] and Maskens[63b] and conforms to the usage employed by most groups working on aldol-type reactions. The convention is as follows: If the main chain is written in an extended, zig-zag conformation, then the diastereomer in which both the C_α substituent and the C_β hydroxy are toward or away from the viewer is the erythro diastereomer. (a) Heathcock, C. H.; Buse, C. T.; Kleischick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066. (b) Maskens, K.; Polger, N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 109. (c) See also: Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106.

(64) Supplemental material in ref 60c.

(65) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(66) Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87.

(67) Literature boiling points of ethyl α-(trimethylsilyl)acetate are: 76–77 °C (40 mm)[38] and 75.5 °C (42 mm).[68]

(68) Gold, J. R.; Sommer, L. H.; Whitmore, F. C. *J. Am. Chem. Soc.* **1948**, *70*, 2874.

(69) Fessenden and Fessenden[38] could not get a satisfactory elemental analysis on ethyl α-(trimethylsilyl)acetate.

Ethyl α-(Diphenylmethylsilyl)acetate. Using the procedure described above for the synthesis of **14**, 2.77 mL (25 mmol) of ethyl α-bromoacetate was coupled with 5.16 mL (25 mmol) of diphenylmethylsilyl chloride in the presence of 1.634 g (25 mmol) of washed zinc metal to afford 6.296 g (89%) of a colorless oil, bp ~166 °C (~1 mm).[38] ^{1}H NMR spectrum matched that in the literature.[38,44]

Ethyl 2-(Trimethylsilyl)-3-methyl-3-butenoate (7). (As a representative example for the formation of α-trimethylsilyl β,γ-unsaturated esters, the synthesis of **7** is described.) Diisopropylamine, 4.20 mL (30 mmol), was dissolved in 5 mL of THF under argon and cooled to −78 °C by means of a dry ice/acetone bath. *n*-Butyllithium (12.30 mL of a 2.44 M solution, 30 mmol) was then added. After the reaction was stirred for 15 min, a solution of 4.57 mL (25 mmol) of ethyl α-(trimethylsilyl)acetate, **14**, in 5 mL of THF was added, and stirring was continued for 30 min at −78 °C.

To a 3-neck flask equipped with an overhead stirrer was added 2.755 g (12.6 mmol) of nickel(II) bromide and 15 mL of THF under argon. This suspension was cooled to −78 °C by means of a dry ice/acetone bath, and 2.05 mL (5 mmol) of 2.44 M *n*-BuLi was added. The resulting black suspension was stirred for 12 min at −78 °C, and 2.66 mL (30 mmol) of 2-bromopropene was then added followed by the lithium enolate of ethyl α-(trimethylsilyl)acetate, formed above, which was transferred via Teflon tubing under argon pressure. The mixture was stirred at −78 °C for 5 min and was then allowed to warm to room temperature until GLC analysis indicated that the reaction was complete (1–4 h). After being recooled to −78 °C, the reaction was quenched by the addition of 100 mL of 5% HCl with stirring, and was then allowed to return to room temperature. The product was extracted with ether and washed three times with 100-mL portions of water, each of the aqueous layers being extracted with fresh ether. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered through 5 mm of neutral alumina topped with 1 cm of Celite in a 150 mL sintered glass funnel, and concentrated to yield 4.3085 g of a brown oil. Fractional distillation in vacuo over a trace of K_2CO_3, using a 6-in. Vigreux column and rapid stirring, afforded 3.123 g (62%) of pure **7** as a nearly colorless oil: bp ~76 °C (~14 mm); ^{1}H NMR (CCl_4) δ 4.83–4.70 (m, 2 H), 4.03 (q, J = 7.2 Hz, 2 H), 2.78 (s, 1 H), 1.78 (s, 3 H), 1.22 (t, J = 7.2 Hz, 3 H), 0.07 (s, 9 H); IR (CCl_4) 1722, 1251, 1148, 1045, 900, 884, 855; mass spectrum (10 eV), m/e (%) 200 (M^+, 5.3), 185 (12.9), 82 (100), 73 (35.3); HRMS calcd for $C_{10}H_{20}O_2Si$, 200.1233; found, 200.1233.

Anal. Calcd for $C_{10}H_{20}O_2Si$: C, 59.95; H, 10.06. Found: C, 59.63 H, 9.92.

Flash chromatography on the crude material from a 5-mmol scale run, using a 43-mm diameter column and 5% ether/hexane as eluent, afforded pure **7** in 74% yield.

Ethyl 2-(Trimethylsilyl)-4-phenyl-3-butenoate (8). By the use of the general method, the enolate of **14** (4.57 mL, 25 mmol) was coupled with 3.37 mL (26.25 mmol) of β-bromostyrene to afford, after flash chromatography on $^1/_{10}$ of the crude material (30 mm diameter column, 1.5% ethyl acetate/hexane as eluent), 211 mg (42%) of **8** as a yellow oil: ^{1}H NMR (CCl_4) 7.38–7.18 (m, 5 H), 6.48 (dd, J = 10.2, 16 Hz, 1 H), 6.26 (d, J = 16 Hz, 1 H), 4.17 (q, J = 7.1 Hz, 2 H), 3.08 (d, J = 10.2 Hz, 1 H), 1.29 (t, J = 7.1 Hz, 3 H), 0.14 (s, 9 H); mass spectrum (10 eV), m/e (%) 262 (M^+, 16.9), 144 (100), 73 (26); HRMS calcd for $C_{15}H_{22}O_2Si$, 262.1389; found, 262.1390.

Ethyl (3*Z*)-2-(Trimethylsilyl)-3-pentenoate (9a). By the use of the general method, the enolate of **14** (4.57 mL, 25 mmol) was coupled with 2.35 mL (27.5 mmol) of 98% *cis*-1-bromo-1-propene to afford, after flash chromatography on $^1/_2$ of the crude material (40 mm diameter column, 4% ethyl acetate/hexane as eluent), 146 mg (8%) of **9a** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 5.71–5.07 (m, $J_{3,4}$ = 11 Hz, 2 H), 4.03 (q, J = 7 Hz, 2 H), 3.00 (d, J = 10.5 Hz, 1 H), 1.49 (dd, J = 2, 6 Hz, 3 H), 1.17 (t, J = 7 Hz, 3 H), 0.02 (s, 9 H).

Ethyl (3*E*)-2-(Trimethylsilyl)-3-pentenoate (10a). By use of the general method, the enolate of **14** (3.97 mL, 21.72 mmol) was coupled with 1.88 mL (21.93 mmol) of 79% *cis*-1-bromo-1-propene to afford, after flash chromatography, 80 mg (4%) of an 8:15 ratio of **9a**:**10a**.

10a: ^{1}H NMR ($CDCl_3$) δ 5.7–4.93 (m, 2 H), 3.95 (q, J = 7.2 Hz, 2 H), 2.62 (d, J = 9 Hz, 1 H), 1.62 (d, J = 6 Hz, 3 H), 1.17 (t, J = 7.2 Hz, 3 H), 0.02 (s, 9 H); mass spectrum on isomer mixture (10 eV), m/z (%) 200 (M^+, 6.4), 82 (100), 75 (11.4), 73 (23.6).

Ethyl 2-(Trimethylsilyl)-3-methyl-3-pentenoate (11). By use of the general method, the enolate of **14** (9.91 mL, 5 mmol) was coupled with 0.53 mL (5.25 mmol) of 2-bromo-2-butene to afford, after flash chromatography (43 mm diameter column, 5% ether/hexane), 347 mg (32%) of a nearly colorless oil. An 80:20 isomeric mixture (GLC analysis) of halide was used, affording isomeric **11**, predominant in the trans isomer (*i.e.*, *cis*-methyls). *trans*-**11**: ^{1}H NMR ($CDCl_3$) δ 5.34 (q, J = 8 Hz, 1 H), 4.10 (q, J = 7.2 Hz, 2 H), 2.84 (s, 1 H), 1.77 (s, 3 H), 1.65 (d, J = 8 Hz, 3 H), 1.32 (t, J = 7.2 Hz, 3 H), 0.15 (s, 9 H). *cis*-**11**: ^{1}H NMR ($CDCl_3$) δ 5.30 (q, J = 7 Hz, 1 H), 4.10 (q, J = 7.2 Hz, 2 H), 3.36 (s, 1 H), 1.90 (s, 3 H), 1.57 (d, J = 7 Hz, 3 H), 1.32 (t, J = 7.2 Hz, 3 H), 0.18 (s, 9 H); mass spectrum on isomer mixture (70 eV), m/z (%) 214 (M^+, 5.2), 96 (100), 75 (28.2), 73 (77.2).

Ethyl 4,4-Bis(trimethylsilyl)acetoacetate (15). By use of the general method for the synthesis of α-trimethylsilyl β,γ-unsaturated esters, the enolate of **14** (5.49 mL, 30 mmol) was coupled with 3.35 mL (33 mmol) of 2-bromo-2-butene to afford, after flash chromatography (65 mm diameter column, ether/CH_2Cl_2/hexane (1:3:16) as eluent), 760 mg (12%) of isomeric **11** along with 871 mg (11%) of **15** as a yellow oil. Purification of 74 mg of the latter material on an 0.2-mm silica gel plate afforded 57 mg (77%) of a nearly colorless oil: ^{1}H NMR (CCl_4) δ 4.18 (q, J = 7 Hz, 2 H), 3.29 (s, 2 H), 2.39 (s, 1 H), 1.36 (t, J = 7 Hz, 3 H), 0.22 (s, 9 H); IR (CCl_4) 3027, 1737, 1672, 1309, 1266, 1256, 1233, 1150, 1032, 872, 847, 837; mass spectrum (10 eV), m/e (%) 274 (M^+, 1.5), 259 (36.1), 187 (100), 147 (51.2), 99 (27.7), 75 (23.1), 73 (62.2); HRMS calcd for $C_{11}H_{23}O_3Si_2$ ($M^+ - CH_3$), 259.1185; found, 259.1187.

Treatment of 7 with LDA. To a solution of 0.11 mL (0.79 mmol) of diisopropylamine in 1 mL of THF under N_2 at −78 °C was added 0.50 mL of 1.58 M *n*-BuLi (0.79 mmol). After the reaction was stirred for 15 min, a solution of 150 mg (0.75 mmol) of **7** in 2 mL of THF was added. After 45 min at −78 °C, the reaction was quenched with aqueous ammonium chloride and extracted with ether. The extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator to yield a yellow oil. After the last traces of solvent were removed under high vacuum, 83 mg (55%) of a yellow oil remained. ^{1}H NMR and GLC analyses indicated the presence of **7** along with a trace of protodesilylated material, viz., ethyl senecioate, no α-trimethylsilyl α,β-unsaturated ester being detected.

Ethyl 2-(Trimethylsilyl)-2,3-dimethyl-3-butenoate (12). Alkylation of 7 with Methyl Iodide. The procedure described above for the treatment of **7** with LDA was followed: 0.645 g (3.22 mmol) of **7** was alkylated with 0.21 mL (3.38 mmol) of methyl iodide to afford, after flash chromatography (30-mm diameter column, 2% ethyl acetate/hexane as eluent), 0.320 g (46%) of **12** as a colorless, volatile oil: ^{1}H NMR ($CDCl_3$) δ 4.82 (br s, 1 H), 4.67 (br s, 1 H), 4.11 (q, J = 7.1 Hz, 2 H), 1.77 (s, 3 H), 1.31 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 0.79 (s, 9 H); mass spectrum (10 eV), m/z (%) 214 (M^+, 4.6), 199 (38.2), 96 (100), 75 (21.6), 73 (79.0); HRMS calcd for $C_{11}H_{22}O_2Si$, 214.1389; found, 214.1390.

***tert*-Butyl Bis(trimethylsilyl)acetate (18).** The reagent was synthesized following the procedure of Hartzell and Rathke.[41,70] ^{1}H NMR ($CDCl_3$) δ 1.79 (s, 1 H), 1.45 (s, 9 H), 0.16 (s, 9 H); IR (CCl_4) 1700, 1692, 1367, 1277, 1252, 1147, 1108, 700–900; mass spectrum (10 eV), m/z (%) 245 ($M^+ - CH_3$, 1.0), 189 (39.4), 147 (100), 75 (52.3), 73 (34.1).

***tert*-Butyl 2-(Trimethylsilyl)-2-pentenoate (19).** To a solution of 0.99 7L (7.04 mmol) of diisopropylamine in 5 mL of THF under N_2 at −78 °C was added 3.16 mL of 2.23 M *n*-BuLi (7.04 mmol). After this reaction was stirred for 25 min, a solution of 1.668 g (6.4 mmol) of **18** in 5 mL of THF was added, and stirring was continued at −78 °C for 1 h. Propionaldehyde (0.51 mL, 7.04 mmol) was added to this solution, and stirring at −78 °C was continued for 4 h at which time the reaction was slowly warmed to room temperature and maintained an additional 13 h. The reaction was quenched by the addition of 10 mL of cold 5% HCl, and the products were extracted into ether. The extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated to yield 2.537 g of a yellow oil. Flash chromatography, using a 65 mm diameter column and 5% ether/hexane as eluent, afforded 1.253 g (86%) of the two geometrical isomers of **19** as colorless, volatile oils.

(*E*)-**19**: ^{1}H NMR (CCl_4) δ 6.04 (t, *J* = 7.2 Hz, 1 H), 2.40 (dq, *J* = 7.2, 7 Hz, 2 H), 1.56 (s, 9 H), 1.11 (t, *J* = 7 Hz, 3 H), 0.14 (s, 9 H); IR (CCl_4) 1708, 1369, 1354, 1248, 1224, 1162, 1142, 842; mass spectrum (10 eV), *m/z* (%) 172 ($M^+ - C_4H_8$, 12.4), 157 (75.7), 156 (67.6), 155 (29.3), 75 (72.8), 73 (18.8), 57 (73.0); HRMS calcd for $C_7H_{13}O_2Si$, 157.0685; found, 157.0682.

(*Z*)-**19**: ^{1}H NMR (CCl_4) δ 6.98 (t, *J* = 7.75 Hz, 1 H), 2.32 (dq, *J* = 7.75, 7.5 Hz, 2 H), 1.56 (s, 9 H), 1.16 (t, *J* = 7.5 Hz, 3 H), 0.31 (s, 9 H); IR (CCl_4) 1703, 1691, 1367, 1273, 1249, 1162, 1148, 852, 840; mass spectrum (10 eV), *m/z* (%) 157 (100), 156 (23.5), 155 (20.3), 75 (65.2), 73 (26.1), 57 (77).

***tert*-Butyl (3*E*)-2-(Trimethylsilyl)-3-pentenoate (10b).** To a solution of 0.30 mL (2.16 mmol) of diisopropylamine in 3 mL of THF under N_2 at −40 °C was added 0.97 mL of 2.23 M *n*-BuLi (2.16 mmol). After 12 min, a solution of 0.496 g (2.17 mmol) of **19** in 3 mL of THF was added, and after being stirred at −40 °C for 5.5 h, the reaction was quenched with aqueous ammonium chloride and extracted with ether. The extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated to yield 1.075 g of a light yellow oil. GLC and NMR analyses indicated a 1.0:1.7 ratio of starting material to product. Flash chromatography, using a 33 mm diameter column and 5% ether/hexane, afforded 235 mg (47%) of **19** and 197 mg (75% conversion yield) of **10b** as a colorless, volatile oil: ^{1}H NMR ($CDCl_3$) δ 5.51 (dd, *J* = 10, 15 Hz, 1 H), 5.21 (dq, *J* = 15, 6 Hz, 1 H), 2.63 (d, *J* = 10 Hz, 1 H), 1.72 (d, *J* = 6 Hz, 3 H), 1.44 (s, 9 H), 0.07 (s, 9 H); mass spectrum (10 eV), *m/z* (%) 172 ($M^+ - C_4H_8$, 100), 157 (32.0), 156 (61.8), 82 (87.3), 75 (30.3), 73 (9.2), 57 (41.7).

General Method for Electrophilic Substitution of α-Silyl β,γ-Unsaturated Esters. Procedure A ($TiCl_4$). As a representative example, the reaction of **7** with chloromethyl phenyl sulfide (**46**) promoted by $TiCl_4$ is described. A 2-necked flask equipped with a Teflon stopcock in place of a third neck was placed under N_2 and charged with 2 mL of CH_2Cl_2, and 0.18 mL (1.63 mmol) of $TiCl_4$ was injected through the stopcock via a syringe. After the vessel was cooled to −78 °C, 0.22 mL (1.63 mmol) of **46** was added followed by 0.297 g (1.48 mmol) of **7** in 3 mL of CH_2Cl_2. The reaction was stirred for 15 min at −78 °C and then at 0 °C for 23.75 h before being quenched with 10 mL of water. The products were extracted into ether, and the extracts were washed with 10 mL each of aqueous sodium bicarbonate and brine, dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator to yield 0.351 g of a yellow oil, partially crystalline. GLC analysis indicated a 1.0:2.1:1.7 ratio of protodesilylated material:*cis*-**38**:*trans*-**38**. Preparative thin-layer chromatography of 270 mg of crude material (3 developments using 1:1 CH_2Cl_2/hexane) afforded 123 mg (52% isolated yield) of the two geometrical isomers of **38**.

(*Z*)-**38**: ^{1}H NMR ($CDCl_3$) δ 7.38–7.36 (m, 2 H), 7.31–7.26 (m, 2 H), 7.19–7.15 (m, 1 H), 5.72 (br s, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.10–3.06 (m, 2 H), 2.95–2.90 (m, 2 H), 1.92 (d, *J* = 1.3 Hz, 3 H), 1.26 (t, *J* = 7.1 Hz, 3 H); mass spectrum (10 eV), *m/z* (%) 250 (M^+, 21.9), 141 (89.4), 123 (100), 113 (54.3), 45 (30.8); HRMS calcd for $C_{14}H_{18}O_2S$, 250.1028; found, 250.1034.

Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.165; H, 7.25; S, 12.81. Found: C, 67.26; H, 7.07; S, 13.79.

(*E*)-**28**: ^{1}H NMR ($CDCl_3$) δ 7.38–7.18 (m, 5 H), 5.69–5.67 (m, 1 H), 4.15 (q, *J* = 7.1 Hz, 2 H), 3.08–2.99 (m, 2 H), 2.47–2.42 (m, 2 H), 2.16 (d, *J* = 1.3 Hz, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H); mass spectrum (10 eV), *m/z* (%) 250 (M^+, 14.1), 141 (65.6), 123 (100), 113 (37.6), 45 (29.9); HRMS calcd for $C_{14}H_{18}O_2S$, 250.1028; found, 250.1032.

Procedure B (Me_3SiOTf). As a representative example, the Me_3SiOTF-catalyzed reaction of **7** with acetone dimethyl acetal is described. To 0.365 g (0.16 mmol) of Me_3SiOTf under argon at −78 °C was added a solution of 0.409 g (2.04 mmol) of **7** in 2 mL of CH_2Cl_2, followed by a solution of 0.25 mL (2.05 mmol) of acetone dimethyl acetal in 2 mL of CH_2Cl_2. The solution was stirred at −78 °C until complete reaction was evident by GLC analysis (26 h). The solution was poured into a separatory funnel containing 10 mL of saturated $NaHCO_3$ and extracted with ether. The organic layer was washed with 10 mL of brine, dried ($MgSO_4$), filtered, and concentrated to yield 0.432 g of a very pale yellow oil. GLC analysis indicated 27% as **7** and two product peaks in a ratio of 14:86. Thick-layer chromatography (five developments, 15% ether/hexanes) afforded a combined yield of 0.262 g (83%, adjusted for recovered **7**) of the pure isomers of ethyl 3,5-dimethyl-5-methoxy-2-hexenoate (**32**).

(*E*)-**32**: ^{1}H NMR (CCl_4) δ 5.52 (m, 1 H), 4.05 (q, *J* = 7 Hz, 2 H), 3.13 (s, 3 H), 2.22 (s, 2 H), 2.16 (d, *J* = 1.5 Hz, 3 H), 1.25 (t, *J* = 7 Hz, 3 H), 1.14 (s, 6 H); mass spectrum (70 eV), *m/z* (%) no M^+, 185 (0.6), 155 (0.6), 74 (4.7), 73 (100).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.62; H, 9.91.

(*Z*)-**32**: ^{1}H NMR (CCl_4) δ 5.63 (m, 1 H), 4.02 (q, *J* = 7 Hz, 2 H), 3.14 (s, 3 H), 2.86 (s, 2 H), 1.94 (br s, 3 H), 1.24 (t, *J* = 7 Hz, 3 H), 1.15 (s, 6 H).

Reaction of 7 with Hexanal. Procedure A was followed using 0.22 mL (2.0 mmol) of $TiCl_4$, 0.30 mL (2.5 mmol) of hexanal, and 0.401 g (2.0 mmol) of **7**. The reaction mixture was stirred at −78 °C for 12 h, then at −30 °C for 3 h. Normal workup afforded 0.391 g of a yellow oil. GLC analysis indicated two products in a ratio of 8:92. Thick-layer chromatography (two developments, 20% ether/hexanes) afforded 81.5 mg (22%) of pure ethyl (*E*)-3-methyl-5-hydroxy-2-decenoate (**21**) as a nearly colorless oil: ^{1}H NMR (CCl_4) δ 5.72–5.55 (m, 1 H), 4.07 (q, *J* = 7.2 Hz, 2 H), 3.92–3.38 (m, 1 H), 2.35–2.08 (m, 2 H), 2.15 (d, *J* = 2 Hz, 3 H), 1.93 (d, *J* = 1 Hz, 1 H), 1.71–1.12 (m, 11 H), 1.05–0.75 (m, 3 H); mass spectrum (70 eV), *m/z* (%) no M^+, 183 (7.52), 128 (100), 100 (59.1), 83 (53.1), 82 (58.9).

Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.39; H, 10.595. Found: C, 68.44; H, 10.55.

Reaction of 7 with Hexanal Promoted by TiF_4. Procedure A was followed using 0.300 g (2.42 mmol) of TiF_4 in place of $TiCl_4$, 0.29 mL (2.42 mmol) of hexanal, and 0.441 g (2.2 mmol) of **7**. The reaction mixture was stirred at −78 °C for 5 h, then allowed to warm to room temperature for 22 h. Usual workup afforded 0.442 g of a yellow oil. Chromatography on a 2-mm phosphate-buffered plate (276 mg crude, four developments, 15% ether/hexane as eluent) afforded 104 mg of a light yellow oil consisting of (*E*)-**21** and the α-dihydropyrone **22** in an 84:16 ratio and 57 mg of a colorless oil of undetermined structure.

22: ^{1}H (CCl_4) δ 5.79 (s, 1 H), 4.40–4.32 (m, 1 H), 2.32 (dd, *J* = 11.7, 17 Hz, 1 H), 2.17 (dd, *J* = 17, 3.9 Hz, 1 H), 1.98 (s, 3 H), 1.82–1.21 (m, 8 H), 0.92–0.86 (m, 3 H); mass spectrum (10 eV), *m/z* (%) 182 (M^+, 2.2), 111 (100), 82 (33.4); HRMS calcd for $C_{11}H_{18}O_2$, 182.1307; found, 182.1305.

Reaction of 7 with *p*-Anisaldehyde. Procedure A was followed using 0.179 mL (1.63 mmol) of $TiCl_4$, 0.198 mL (1.63 mmol) of *p*-anisaldehyde, and 0.297 g (1.48 mmol) of **7**. The reaction mixture was stirred for 23.5 h at −78 °C before workup. GLC analysis indicated 19% anisaldehyde and two product peaks in a ratio of 18:82. Thick-layer chromatography on a phosphate-buffered plate (five developments, 20% ether/hexanes) afforded a combined total of 0.242 g (62%) of mixtures of geometrical isomers of diethyl 3,7-dimethyl-5-(4-methoxyphenyl)-2,8-nonadien-1,9-dioate (**23**) and *p*-anisaldehyde. Repeated thin-layer chromatographies afforded pure *trans,trans*-**23** and *cis,trans*-**23** contaminated with *p*-anisaldehyde.

(*E,E*)-**23**: ^{1}H NMR (CCl_4) δ 6.99 (d, *J* = 8.7 Hz, 2 H), 6.77 (d, *J* = 8.7 Hz, 2 H), 5.50 (s, 2 H), 4.07 (q, *J* = 7.1 Hz, 4 H), 3.76 (s, 3 H), 3.02 (tt, *J* = 6.4, 8.65 Hz, 1 H), 2.41 (dd, *J* = 6.4, 13.4 Hz, 2 H), 2.33 (dd, *J* = 8.65, 13.4 Hz, 2 H), 2.06 (d, *J* = 1.2 Hz, 6 H), 1.24 (t, *J* = 7.1 Hz, 6 H); mass spectrum (70 eV), *m/z* (%) 374 (M^+, 5), 329 (5.1), 247 (100), 201 (74.7), 173 (30.1).

(*Z,E*)-**23**: ^{1}H NMR (CCl_4) δ 7.04 (d, *J* = 8.6 Hz, 2 H), 6.75 (d, *J* = 8.6 Hz, 2 H), 5.59 (s, 1 H), 5.51 (s, 1 H), 4.14–4.04 (m, 4 H), 3.76 (s, 3 H), 3.1–3.01 (m, 2 H), 2.41 (apparent dt, *J* = 3.1, 11.1, Hz, 1 H), 2.5–2.37 (m, 2 H), 2.07 (d, *J* = 1.2 Hz, 3 H), 1.64 (d, *J* = 1.3 Hz, 3 H), 1.29–1.22 (m, 6 H); mass spectrum (70 eV), *m/z* (%) 374 (M^+, 2.4), 329 (4.2), 247 (56.1), 201 (100), 173 (14.1); HRMS calcd for $C_{22}H_{30}O_5$, 374.2093; found, 374.2089.

Reaction of 7 with *p*-Nitrobenzaldehyde. To a two-neck flask equipped with a Teflon stopcock (instead of a third neck) under nitrogen was added 0.249 g (1.65 mmol) of *p*-nitrobenzaldehyde and 3 mL of CH_2CL_2. After the vessel was cooled to −78 °C, 0.181 mL (1.65 mmol) of $TiCl_4$ was injected through the Teflon stopcock followed by the addition of a solution of 0.3005 g (1.5 mmol) of **7** in 2 mL of CH_2Cl_2. The reaction was stirred at −78 °C for 16 h before workup. ^{1}H NMR analysis of the crude product indicated only the trans isomer. Thick-layer chromatography on a phosphate-buffered plate (five developments, 5%

EtOAc/benzene) afforded 0.313 g (75%) of slightly impure ethyl (*E*)-3-methyl-5-hydroxy-5-(4-nitrophenyl)-2-pentenoate (**24**) as a yellow oil which slowly became crystalline. Recrystallization of 174 mg of crude **24** from CCl_4 afforded 110 mg (65%) of very pale yellow cubic crystals: mp 76.5–78.5 °C; ^1H NMR (CCl_4) δ 8.16 (d, J = 8.5 Hz, 2 H), 7.48 (d, J = 8.5 Hz, 2 H), 5.65 (s, 1 H), 5.03–4.81 (m, 1 H), 4.08 (q, J = 7.2 Hz, 2 H), 2.44 (d, J = 6.2 Hz, 2 H), 2.38 (d, J = 3.2 Hz, 1 H), 2.19 (s, 3 H), 1.26 (t, J = 7.2 Hz, 3 H); mass spectrum (70 eV), m/z (%) no M^+, 234 (5.9), 152 (18), 128 (100), 100 (50.7), 83 (42.3), 82 (56.5).

Anal. Calcd for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.135; N, 5.015. Found: C, 60.26; H, 6.09; N, 4.74.

Reactions of 7 with *p*-Nitrobenzaldehyde Promoted by $FeCl_3$. To a two-neck flask under argon was added 0.132 g (0.81 mmol) of $FeCl_3$ in 1 mL of CH_2Cl_2. After the vessel was cooled to −78 °C, a solution of 0.123 g (0.81 mmol) of *p*-nitrobenzaldehyde and 0.148 g (0.74 mmol) of **7** in 5 mL of CH_2Cl_2 was then added dropwise. The reaction was stirred at −78 °C for 4 h and then allowed to warm slowly to room temperature over a period of 13.5 h. After the usual workup and preparative thin-layer chromatography (two developments, 5% ethyl acetate/benzene as eluent), a combined yield of 0.156 g (86%) of diastereomeric 2,6-bis(4-nitrophenyl)-3-(ethoxycarbonyl)-4-methyl-4-chloro-4*H*-tetrahydropyran (**37**) was obtained. The higher R_f component, 0.111 g, existed as a nearly colorless foam whereas the lower R_f band, 0.045 g, was obtained as a yellow oil and consisted of several diastereomeric components. Higher R_f diastereomer: ^1H NMR ($CDCl_3$) δ 8.21 (dd, J = 2.5, 8.5 Hz, 4 H), 7.61 (dd, J = 9, 11 Hz, 4 H), 5.28 (d, 10.5 Hz, 1 H), 5.26 (dd, J = 2.5, 11 Hz, 1 H), 4.04 (q, J = 7 Hz, 2 H), 2.88 (d, J = 10.5 Hz, 1 H), 2.40 (dd, J = 2.5, 14 Hz, 1 H), 2.07 (dd, J = 11, 14 Hz, 1 H), 1.84 (s, 3 H), 1.11 (t, J = 7 Hz, 3 H); mass spectrum (10 eV), m/z (%) 450 (M^+ + 2, 0.8), 488 (M^+, 3.9), 366 (25), 263 (100), 262 (59.4).

Treatment of 37 with 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU). A solution of the diastereomeric mixture of **37** (32 mg, 0.07 mmol) and 11 μL (0.07 mmol) of DBU in 1 mL of THF was brought to reflux for 2.5 h. After being cooled, the reaction was quenched with aqueous ammonium chloride, and the products were extracted with chloroform. The extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated to yield 44 mg of a brown oil. Thin-layer chromatography (one development, 7% ethyl acetate/benzene as eluent) afforded 3 mg (10%) of 2,6-bis(4-nitrophenyl)-3-(ethoxycarbonyl)-4-methyl-5,6-dihydro-α-pyran (**53**) as a golden orange oil: ^1H NMR ($CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 4 H), 7.64–7.44 (m, 4 H), 5.78–5.67 (m, 1 H), 5.01–4.76 (m, 1 H), 3.96 (q, J = 7 Hz, 2 H), 2.64–2.41 (m, 2 H), 2.22 (br s, 3 H), 1.03 (t, J = 7 Hz, 3 H); mass spectrum (10 eV), m/z (%) 412 (M^+, 23.7), 366 (100), 339 (29.3), 261 (26.3).

Reaction of 7 with Benzoyl Chloride. Procedure A was followed using 0.365 mL (3.32 mmol) of $TiCl_4$, 0.385 mL (3.32 mmol) of benzoyl chloride, and 0.605 g (3.02 mmol) of **7**. The reaction was run at −30 °C and maintained for 5 h then warmed to room temperature for 43 h before workup. GLC analysis indicated that the reaction was incomplete and that there were four products in the ratio of 5:19:4:72. Thick-layer chromatography afforded impure 4-methyl-6-phenyl-2*H*-2-pyranone (**26**) as the predominant component and the isomers of ethyl 3-methyl-5-oxo-5-phenyl-2-pentenoate (**25**) contaminated with an unidentified component. Repeated chromatography of the isomer mixture failed to separate the isomers or the unknown. Recrystallization from ether/hexanes, however, afforded pure **26** as pale yellow needles: mp 85–86.5 °C (lit.[71]).

26: ^1H NMR (CCl_4) δ 7.8–7.6 (m, 2 H), 7.5–7.2 (m, 3 H), 6.40 (d, J = 1 Hz, 1 H), 5.88 (d, J = 1 Hz, 1 H), 2.12 (s, 3 H); mass spectrum (70 eV), m/z (%) 186 (M^+, 88.2), 158 (100), 129 (37.9), 115 (19.3), 105 (39.8), 77 (44); HRMS calcd for $C_{12}H_{10}O_2$, 186.0681; found, 186.0684. The infrared spectrum matched that in the literature.[70]

Mixture of (*E*)- and (*Z*)-**25** (plus the unknown): ^1H NMR δ 8.03–7.8 (m), 7.53–7.2 (m), 6.8 (m), 5.75 (m), 4.37 (br s), 4.1 (q, J = 7 Hz), 4.07 (q, J = 7 Hz), 3.7 (s), 3.64 (s), 3.14 (br s), 2.21 (br s), 2.07 (d, J = 1 Hz), 1.97 (d, J = 1 Hz), 1.4–1.03 (m); mass spectrum (70 eV), m/z (%) 232 (M^+, 4.8), 158 (18), 105 (100), 84 (31.1), 77 (32.5), 49 (35.4).

Reaction of 7 with Trimethylacetyl Chloride. Procedure A was followed using 0.306 mL (3.28 mmol) of $TiCl_4$, 0.404 mL (3.28 mmole of trimethylacetyl chloride, and 0.597 g (2.98 mmol) of **7**. The reaction was stirred at −78 °C for 5 min and then at room temperature for 23.5 h before workup. GLC analysis indicated four peaks in a ratio of 55:22:18:6. Thick-layer chromatography of 325 mg of crude material (four developments, 15% ether/hexanes) afforded a combined total of 212 mg (58%), which consisted of 193 mg of a mixture of the two isomers of ethyl 3,6,6-trimethyl-5-oxo-2-heptenoate (**27**) contaminated with an unidentified component and 19 mg of 4-methyl-6-*tert*-butyl-2-pyranone (**28**). Repeated thin-layer chromatography of the isomer mixture afforded pure (*Z*)-**27** and (*E*)-**27** contaminated with the unknown.

(*Z*)-**27**: ^1H NMR (CCl_4) δ 5.69 (m, 1 H), 4.02 (q, J = 7 Hz, 2 H), 3.85 (br s, 2 H), 1.88 (d, J = 1.5 Hz, 3 H), 1.22 (t, J = 7 Hz, 3 H), 1.16 (s, 9 H); mass spectrum (70 eV), m/z (%) 212 (M^+, 1.5), 167 (7.6), 155 (35.9), 127 (37.4), 85 (29.6), 57 (100); HRMS calcd for $C_{12}H_{20}O_3$, 212.1412; found, 212.1416.

(*E*)-**27** (plus the unknown): ^1H NMR (CCl_4) δ 6.3 (m, 1 H), 6.25 (m, 1 H), 5.49 (m, 1 H), 4.06 (q, J = 7 Hz, 4 H), 3.47 (s, 1 H), 3.2 (s, 1 H), 3.0 (s, 2 H), 2.09 (br s, 3 H), 1.93 (d, J = 1.5 Hz, 3 H), 1.27 (t, J = 7 Hz, 3 H), 1.26 (t, J = 7 Hz, 3 H), 1.14 (s, 9 H), 1.11 (s, 9 H); mass spectrum (70 eV), m/z (%) 212 (M^+, 1.7), 167 (10.6), 155 (62.5), 127 (81.5), 84 (21.5), 57 (100); HRMS calcd for $C_{12}H_{20}O_3$, 212.1412; found, 212.1413.

4-Methyl-6-*tert*-butyl-2-pyrone (28). The reaction of **7** with trimethylacetyl chloride was repeated, following Procedure A, using 0.363 mL (3.3 mmol) of $TiCl_4$, 0.388 mL (3.15 mmol) of trimethylacetyl chloride, and 0.601 g (3.0 mmol) of **7**. The raction mixture was stirred at −78 °C for 15 min and then at room temperature for 54.5 h before workup. GLC analysis indicated a mixture of the two isomers of **27**, **28**, and the unidentified component. This mixture was dissolved in 4 mL of absolute ethanol under nitrogen and sodium ethoxide, 0.302 mL of a 1 M solution (0.302 mmol) in ethanol, was added. The reaction was stirred at room temperature for 12.3 h and was then quenched with saturated ammonium chloride. After solvent removal in vacuo, the product was extracted with ether, and the organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated to afford 0.442 g (89% from **7**) of impure **28**. Thick-layer chromatography (two developments, 5% ether/CH_2Cl_2) on 141 mg of crude **28** afforded pure **28** in an overall yield of 74% from **7**.

28: ^1H NMR (CCl_4) δ 5.8 (d, J = 1.5 Hz, 1 H), 5.73 (d, J = 1.5 Hz, 1 H), 2.08 (s, 3 H), 1.24 (s, 9 H); IR (CCl_4) 1760–1700, 1563, 1103.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.17; H, 8.39.

Reaction of 7 with Acetone. Procedure A was followed using 0.605 mL (5.5 mmol) of $TiCl_4$, 0.404 mL (5.5 mmol) of acetone, and 1.002 g (5.0 mmol) of **7**. The reaction was stirred at −78 °C for 15 min and then warmed to room temperature for 23.5 h before workup. GLC analysis indicated two peaks in a ratio of 10:90, the latter peak partially unstable. Thick-layer chromatography of 391 mg of crude material on a phosphate-buffered plate (nine developments, 7% ether/hexanes) afforded a combined yield of 0.238 g (~60%), which consisted of 35 mg of ethyl 3,5-dimethyl-5-chloro-2-hexenoate (**31**) along with products resulting from dehydrochlorination and 203 mg of a mixture of ethyl (*E*)-3,5-dimethyl-5-hydroxyl-2-hexenoate (**29**) and 4,6,6-trimethyl-5,6-dihydro-2*H*-pyran-2-one (**30**). Thin-layer chromatography of the latter mixture on a phosphate-buffered plate (two developments, 5% ether/CH_2Cl_2) afforded pure **29** as a colorless oil and pure **30** as a pale yellow oil.

(*E*)-**31**: ^1H NMR (CCl_4) δ 5.63 (m, 1 H), 4.08 (q, J = 7.2 Hz, 2 H), 2.57 (s, 2 H), 2.24 (d, J = 2 Hz, 3 H), 1.60 (s, 6 H), 1.26 (t, J = 7.2 Hz, 3 H); IR (neat) 1718, 1645, 1227, 1152, 1047; mass

(70) No data other than boiling points were reported[41] for the mono and bis(trimethylsilyl)-substituted *tert*-butyl acetates.

(71) Slightly different data has been reported on 4-methyl-6-phenyl-2-pyranone (**26**): (a) Giraud, M.; Molho, D. *Bull. Soc. Chim. Fr.* **1970** 2751. Reported, mp 86–87 °C, IR ν_{co} 1690 cm^{-1} (KBr), UV λ_{max} 240 nm (ϵ 14 900) and 332 nm (ϵ 23,250) in ethanol. (b) Koshimina, N. V.; Peryeev, F. Ya. *Zh. Org. Khim. (Engl. Trans.)* **1976**, *12*, 2021. Reported, IR (CCl_4, 1%) 1750–1720 (s), 1650 (s), 1560 (s), 1500 (s), 1460 (s), 1440 (s) cm^{-1}; ^1H NMR δ 2.12 (3 H), 5.84 (1 H), 6.38 (1 H), 7.32 (3 H), 7.72 (2 H). (c) Izumi, T.; Kasahara, A. *Bull Chem. Soc., Jpn.* **1975**, *48*, 1673. Reported, mp 88–90 °C.

spectrum (70 eV), *m/z* (%) 206 (M + 2, 2.66), 204 (6.1), 169 (68.8), 168 (73.1), 161 (22), 159 (62.3), 153 (100), 123 (89.5), 100 (77.1), 95 (93.97), 77 (82.7); HRMS calcd for $C_{10}H_{17}O_2Cl$, 204.0917 and 206.0887; found, 204.0927 and 206.0898.

(*E*)-**29**: ^{1}H NMR (CCl_4) δ 5.58 (m, 1 H), 4.07 (q, *J* = 7.2 Hz, 2 H), 2.24 (s, 2 H), 2.21 (s, 3 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 1.19 (s, 6 H); IR (neat) 3460, 1709, 1650, 1385, 1376, 1229, 1152, 1052; mass spectrum (70 eV), *m/z* (%) no M^+, 141 (7.8), 128 (67.4), 100 (58.5), 83 (63.1), 82 (62.4), 59 (100).

Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.36; H, 9.76.

30: ^{1}H NMR (CCl_4) δ 5.68 (m, 1 H), 2.24 (br s, 2 H), 1.92 (br s, 3 H), 1.39 (s, 6 H); IR (CCl_4) 1755–1690, 1381, 1372, 1360, 1287, 1184, 1140, 1132, 995; mass spectrum (70 eV), *m/z* (%) 140 (M^+, 2.8), 125 (22.8), 97 (6.6), 82 (100), 54 (19.2), 43 (59.5).

Synthesis of *p*-Anisaldehyde Di-*n*-butyl Acetal. A mixture of 1.217 mL (0.01 mol of *p*-anisaldehyde, 4.651 g (0.021 mol) of tri-*n*-butyl orthoformate, and 1 mg of *p*-toluenesulfonic acid monohydrate in 5 mL of dry 1-butanol and 5 mL of dry benzene were stirred under nitrogen at 0 °C for 1 h and then at room temperature for 20 h. After removal of the majority of the solvent in vacuo, the mixture was extracted with ether and washed with saturated $NaHCO_3$. The aqueous layer was extracted with ether, and the combined organic layers were washed with saturated $NaHCO_3$ and then brine, dried (Na_2SO_4), and concentrated to yield 2.949 g of impure acetal as a yellow oil. Fractional distillation over K_2CO_3 and discarding a large forerun afforded 1.3835 g (52%) of acetal as a colorless oil: bp 155–158 °C (~2 mm); ^{1}H NMR (CCl_4) δ 7.26 (d, *J* = 8 Hz, 2 H), 6.73 (d, *J* = 8 Hz, 2 H), 5.37 (s, 1 H), 3.75 (s, 3 H), 3.48–3.28 (m, 2 H), 1.64–1.24 (m, 4 H), 1.01–0.81 (m, 6 H); mass spectrum (70 eV), *m/z* (%) 266 (M^+, 2.1), 194 (11.1), 193 (78), 137 (100), 135 (15.2), 109 (10.4), 57 (12.3).

Reaction of 7 with *p*-Anisaldehyde Di-*n*-butyl Acetal. Procedure B was followed using 0.017 g (0.08 mmol) of Me_3SiOTf, 0.3005 g (1.0 mmol) of **7**, and 0.4195 g (1.58 mmol) of *p*-anisaldehyde di-*n*-butyl acetal. The reaction was stirred at −78 °C for 2 h before workup. GLC analysis indicated two peaks in a ratio of 3:97. Thick-layer chromatography of 290 mg of crude material (three developments, 2% ether/CH_2Cl_2) afforded a combined yield of 0.236 g (81%) of the isomers of ethyl 3-methyl-5-(*O*-*n*-butyl)-5-(4-methoxyphenyl)-2-pentenoate (**33**).

E-**33**: ^{1}H NMR (CCl_4) δ 7.20 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.66 (s, 1 H), 4.34 (dd, *J* = 5.1, 8.4 Hz, 1 H), 4.13 (q, *J* = 7.1 Hz, 2 H), 3.81 (s, 3 H), 3.31–3.16 (m, 2 H), 2.61 (dd, *J* = 8.5, 14 Hz, 1 H), 2.36 (dd, *J* = 5, 14 Hz, 1 H), 2.17 (s, 3 H), 1.51–1.46 (m, 2 H), 1.35–1.28 (m, 2 H), 1.26 (t, *J* = 7.1 Hz, 3 H), 0.86 (t, *J* = 7.3 Hz, 3 H); mass spectrum (70 eV), *m/z* (%) no M^+, 247 (1.2), 193 (80.3), 194 (10.7), 138 (10.8), 137 (100), 135 (12.4), 109 (11.9).

Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: 71.22; H, 8.78.

Reaction of 7 with Benzaldehyde Promoted by TiF_4. Procedure A was followed using 0.236 g (1.90 mmol) of TiF_4 in place of $TiCl_4$, 0.19 mL (1.90 mmol) of benzaldehyde, and 0.363 g (1.81 mmol) of **7**. The reaction mixture was stirred for 90 min at −78 °C, 90 min at −32 °C, and then 7 h at room temperature before the usual workup, which yielded 0.489 g of a yellow oil. Chromatography of 254 mg of crude material on a 2-mm phosphate-buffered silica gel plate (6 developments, 7% ether/hexane) afforded 7 mg (3%) of ethyl 3-methyl-5-phenyl-2,4-pentadienoate (**36**), 77 mg (16%) of ethyl 3-methyl-5-phenyl-5-hydroxy-2-pentenoate (**34**), and 74 mg (64%) of bis(5-ethoxy-5-oxo-1-phenyl-3-methyl-3-penten-1-yl) ether (**35**), all as nearly colorless oils.

(*E,E*)-**36**: ^{1}H NMR (CCl_4) δ 7.48–7.26 (m, 5 H), 6.94 (d, *J* = 16.1 Hz, 1 H), 6.81 (d, *J* = 16.1 Hz, 1 H), 5.91 (s, 1 H), 4.2 (q, *J* = 7.1 Hz, 2 H), 2.41 (s, 3 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

E-**34**: ^{1}H NMR (CCl_4) δ 7.35–7.17 (m, 5 H), 5.61 (s, 1 H), 4.2–4.13 (m, 5 H), 2.57 (dd, *J* = 8.9, 13.4 Hz, 1 H), 2.29 (dd, *J* = 4.3, 13.4 Hz, 1 H), 1.99 (s, 3 H), 1.59 (br s, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H); IR (neat) 3610–3106, 1704, 1645, 1225, 1152, 1101–1010; mass spectrum (10 eV), *m/z* (%) no M^+, 128 (100), 107 (31), 100 (26.0), 83 (23.89), 82 (42.5).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.62; H, 7.83.

(*E,E*)-**35**: ^{1}H NMR (CCl_4) δ 7.4–7.2 (m, 10 H), 5.77 (s, 2 H), 4.9 (dd, *J* = 4.7, 8.6 Hz, 2 H), 4.14 (q, *J* = 7.1 Hz, 4 H), 2.6–2.47 (m, 4 H), 2.22 (s, 6 H), 1.27 (t, *J* = 7.1 Hz, 6 H); IR (neat) 1686, 1639, 1217, 1145, 1140, 1080, 1066, 784, 760; mass spectrum (10 eV), *m/z* (%) no M^+, 323 (7.5), 217 (100), 171 (32.2), 143 (15.1); field-desorption mass spectrum, 451 (M^+ + 1).

Anal. Calcd for $C_{28}H_{34}O_5$: C, 74.64; H, 7.61. Found: C, 74.39; H, 7.61.

Treatment of 34 with TiF_4. To a solution of 0.015 g (0.12 mmol) of TiF_4 in 1 mL of CH_2Cl_2 under N_2 at −78 °C was added 0.038 g (0.16 mmol) of **34** in 2 mL of CH_2Cl_2. The reaction mixture was stirred at −78 °C for 24.5 h and at room temperature for 69 h and was quenched with water. The products were extracted into ether, the aqueous layer being neutralized with aqueous sodium bicarbonate before separation. The ether layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated to yield 0.038 g of a yellow oil. GLC, TLC, and ^{1}H NMR analyses indicated a mixture of the diene **36**, starting material **34**, and the ether **35**, the last one being the predominant product.

Reaction of 11 with Chloromethyl Phenyl Sulfide (46). Procedure A was followed using 0.18 mL (1.65 mmol) of $TiCl_4$, 0.21 mL (1.58 mmol) of **46**, and 0.322 g (1.5 mmol) of **11**. The reaction mixture was stirred at −78 °C for 30 min, warmed to 0 °C for 10 h, and then allowed to warm slowly to room temperature and maintained for 11 h. After the usual workup, GLC analysis indicated some protodesilylated material and three sets of products, each set composed of a cis and trans isomer, the latter six in a ratio of 22.3:26.4:1.0:7.8:1.6:6.6. Preparative thin-layer chromatography of 333 mg of crude material (two developments, 1:10:10 ether/CH_2Cl_2/hexane as eluent) afforded 198 mg of an off-white oily solid composed of the three product sets. Preparative thin-layer chromatography of this mixture (three developments, 10% ethyl acetate/hexane as eluent) afforded 64 mg (combined weight, 20%) of the cis and trans isomers of the desired adduct **39** and 54 mg (combined weight, 12%) of the cis and trans isomers of two sets of diadducts **40**, differing in aryl substitution pattern.

(*Z*)-**39**: ^{1}H NMR ($CDCl_3$) δ 7.43–7.07 (m, 5 H), 5.66 (br s, 1 H), 4.32–3.89 (m, 1 H), 4.04 (q, *J* = 7 Hz, 2 H), 2.92 (d, *J* = 8 Hz, 2 H), 1.82 (s, 3 H), 1.37–1.07 (m, 6 H).

(*E*)-**39**: ^{1}H NMR ($CDCl_3$) 7.43–7.07 (m, 5 H), 5.66 (br s, 1 H), 4.12 (q, *J* = 7 Hz, 2 H), 3.19–2.31 (m, 3 H), 2.09 (s, 3 H), 1.37–1.07 (m, 6 H); mass spectrum (10 eV), *m/z* (%) 264 (M^+, 26.2), 155 (100), 127 (22.8), 123 (80.2); HRMS calcd for $C_{15}H_{22}O_2S$, 264.1184; found, 264.1184.

High R_f *E*-**40**: ^{1}H NMR ($CDCl_3$) δ 7.4–7.03 (m, 9 H), 5.63 (br s, 1 H), 4.23 (s, 2 H), 4.1 (q, *J* = 7 Hz, 2 H), 3.13–2.23 (m, 3 H), 2.08 (s, 3 H), 1.36–1.07 (m, 6 H); mass spectrum (10 eV), *m/z* (%) 388 (M^+ + 2, 4.8), 387 (11.7), 386 (M^+, 38.2), 277 (23.0), 155 (100), 123 (39.2).

High R_f (*Z*)-**40**: The ^{1}H NMR differs from that of the *E* isomer only at δ 1.79 (s, 3 H) instead of δ 2.08 (s, 3 H).

Low R_f *E*-**40**: ^{1}H NMR ($CDCl_3$) δ 7.33–6.9 (m, 9 H), 5.61 (br s, 1 H), 4.1 (q, *J* = 7 Hz, 2 H), 4.01 (s, 2 H), 3.1–2.23 (m, 3 H), 2.09 (s, 3 H), 1.36–1.1 (m, 6 H); mass spectrum (10 eV), *m/z* (%) 388 (M^+ + 2, 9.1), 387 (23.8), 386 (M^+, 90.6), 278 (21.1), 277 (100), 232 (33.4), 155 (32.26); HRMS calcd for $C_{22}H_{26}O_2S_2$, 386.1375; found, 386.1364.

Reaction of 11 with Benzaldehyde. Procedure A was followed using 0.181 mL (1.65 mmol) of $TiCl_4$, 0.17 mL (1.65 mmol) of benzaldehyde, and 0.320 g (1.49 mmol) of **11**. The reaction mixture was stirred at −78 °C for 75 min and then warmed to room temperature and allowed to stir for 21.25 h before the usual workup. Chromatography of 390 mg of crude material on a 2-mm phosphate-buffered silica gel plate (one development, 100% CH_2Cl_2 as eluent) afforded 171 mg (combined weights, 44%) of the cis and trans chloro adducts **43** and 66 mg (combined weights, 21%) of the geometrical isomers of ethyl 2-acetylcinnamate (**44**).

(*Z*)-**43**: ^{1}H NMR (CCl_4) δ 7.22 (s, 5 H), 5.43 (br s, 1 H), 4.76 (d, *J* = 9 Hz, 1 H), 4.04 (q, *J* = 7 Hz, 2 H), 2.97–2.56 (m, 1 H), 1.93 (s, 3 H), 1.27 (t, *J* = 7 Hz, 3 H), 1.14 (d, *J* = 6 Hz, 3 H).

(*E*)-**43**: ^{1}H NMR (CCl_4) δ 7.26 (s, 5 H), 5.68 (br s, 1 H), 4.62 (d, *J* = 10 Hz, 1 H), 4.07 (q, *J* = 7 Hz, 2 H), 2.97–2.56 (m, 1 H), 2.16 (s, 3 H), 1.27 (t, *J* = 7 Hz, 3 H), 0.87 (d, *J* = 6 Hz, 3 H); IR (neat) 1706, 1639, 1447, 1221, 1155; mass spectrum (10 eV), *m/z* (%) 266 (M^+, 0.5), 231 (10.9), 141 (86), 127 (32.0), 125 (100); HRMS

calcd for $C_{15}H_{19}O_2Cl$, 266.1074; found, 266.1066.

(*E*)-**44**: ^1H NMR (CCl_4) δ 7.47 (s, 1 H), 7.28 (s, 5 H), 4.19 (q, J = 7 Hz, 2 H), 1.86 (s, 3 H), 1.29 (t, J = 7 Hz, 3 H); IR (CCl_4) 1721, 1705, 1627, 1453, 1371, 1260, 1202, 1187, 1061; mass spectrum (10 eV), m/z (%) 218 (M^+, 100), 217 (79.3), 203 (24.2), 173 (21.4), 131 (38.6).

(*Z*)-**44**: ^1H NMR (CCl_4) δ 7.42 (s, 1 H), 7.37-7.23 (m, 5 H), 4.19 (q, J = 7 Hz, 2 H), 2.26 (s, 3 H), 1.22 (t, J = 7 Hz, 3 H); IR (CCl_4) 1725, 1696, 1666, 1624, 1604, 1382, 1247, 1231, 1202, 1193, 1185, 1043; mass spectrum (10 eV), m/z (%) 218 (M^+, 100), 217 (71.8), 203 (23.6), 173 (22.9), 131 (33.3). Authentic samples of isomeric ethyl 2-acetylcinnamate (**44**) were prepared by Knoevenagel condensation of ethyl acetoacetate with benzaldehyde for spectroscopic comparison.[72] HRMS calcd for $C_{13}H_{14}O_3$, 218.0943; found, 218.0941.

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.16; H, 6.51.

Reaction of 12 with Trimethylacetyl Chloride. Procedure A was followed using 0.04 mL (0.38 mmol) of $TiCl_4$, 0.05 mL (0.38 mmol) of trimethylacetyl chloride, and 0.074 g (0.34 mmol) of **12**. The reaction mixture was stirred at -78 °C for 8 h before being warmed slowly to room temperature and being allowed to stir for 39.5 h. After the usual workup, GLC analysis indicated protodesilylated material and two products. Thin-layer chromatography (one development, 10% ethyl acetate/hexane as eluent) afforded 20 mg (26%) of the δ-keto esters **41** as a peach-colored oil and 5 mg (10%) of the α-pyrone **42** as an apricot-colored oil.

41: mass spectrum (10 eV), m/e (%) 226 (M^+, 32.1), 181 (32.9), 180 (61.5), 169 (100), 142 (57.6), 141 (43.4), 113 (42.4), 85 (100), 57 (100).

42: mass spectrum (10 eV), m/z (%) 180 (M^+, 100), 137 (72.8), 135 (35.7), 123 (34.3), 85 (23.6), 57 (28.4).

Reaction of 8 with *p*-Anisaldehyde Di-*n*-butyl Acetal. Procedure B was followed using 0.012 mg (0.05 mmol) of Me_3SiOTf, 0.420 g (1.58 mmol) of *p*-anisaldehyde di-*n*-butyl acetal, and 0.405 g (1.54 mmol) of **8**. The reaction mixture was stirred at -78 °C for 4.5 h before being warmed to room temperature and allowed to stir for 17 h. The usual workup afforded 0.596 g (100%) of a brown oil. GLC analysis indicated three product peaks and a minor amount of **8** remaining. Preparative thin-layer chromatography of 298 mg of crude material (two developments, 1% ether/CH_2Cl_2 as eluent) afforded 20 mg (20%) of protodesilylated material and 180 mg (60%) of the isomeric adducts **45**. Separation of the latter (5-μm SiO_2 HPLC column, 0.1% 2-propanol/hexane as eluent) afforded two diastereomers in an average ratio of 65:35, the major diastereomer eluting first. A very minor amount of a third diasteromer eluted last, but the quantity isolated was insufficient for characterization. The major isomer is the 2(*E*) adduct **45a**: ^1H NMR (CCl_4) δ 7.26-7.16 (m, 7 H), 6.83 (d, J = 8.5 Hz, 2 H), 6.17 (d, J = 16 Hz, 1 H), 5.91 (dd, J = 8.8, 16 Hz, 1 H), 4.51 (d, J = 10 Hz), 4.32 (q, J = 7.1 Hz, 2 H), 3.77 (s, 3 H), 3.44 (pseudotriplet, J = 9.4 Hz, 1 H), 3.32-3.19 (m, 2 H), 1.50-1.42 (m, 2 H), 1.39-1.26 (m, 5 H), 0.89-0.83 (t, J = 7.2 Hz, 3 H); mass spectrum (10 eV), m/z (%) no M^+, 193 (100), 137 (50.9); field-desorption mass spectrum found $M^+ + 2$, $M^+ + 1$, and weak M^+.

The minor isomer is the 2(*Z*) adduct **45b**: ^1H NMR (CCl_4) δ 7.27-7.05 (m, 7 H), 6.69 (d, J = 8 Hz, 2 H), 6.22 (d, J = 4 Hz, 2 H), 4.44 (d, J = 7.5 Hz, 1 H), 3.86 (q, J = 8 Hz, 2 H), 3.72 (s, 3 H), 3.33-3.11 (m, 3 H), 1.52-1.38 (m, 2 H), 1.38-1.23 (m, 2 H), 1.04 (t, J = 7.3 Hz, 3 H), 0.83 (t, J = 4.5 Hz, 3 H); mass spectrum (10 eV), m/z (%) no M^+, 193 (100), 137 (56.7).

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Registry No. **7**, 82343-39-3; (*E*)-**8**, 87696-52-4; (*Z*)-**9a**, 87696-53-5; (*Z*)-**9b**, 87696-54-6; (*E*)-**10a**, 87696-55-7; (*E*)-**10b**, 87696-56-8; (*E*)-**11**, 87696-57-9; (*Z*)-**11**, 87696-69-3; **12**, 87696-58-0; **14**, 4071-88-9; **15**, 87696-70-6; **18**, 61501-32-4; (*E*)-**19**, 87696-71-7; (*Z*)-**19**, 87696-75-1; (*E*)-21, 82343-40-6; **22**, 87696-59-1; (*E*,*E*)-**23**, 82343-43-9; (*E*,*Z*)-**23**, 82343-44-0; (*E*)-**24**, 82343-45-1; **25**, 82343-51-9; **26**, 4467-30-5; (*E*)-**27**, 87696-60-4; (*Z*)-**27**, 87696-73-9; **28**, 82343-53-1; (*E*)-**29**, 57003-45-9; **30**, 6970-56-5; (*E*)-**31**, 82343-50-8; (*E*)-**32**, 82343-46-2; (*Z*)-**32**, 82343-47-3; (*E*)-**33**, 82343-48-4; (*Z*)-**33**, 82343-49-5; (*E*)-**34**, 57003-46-0; **35**, 87696-61-5; (*E*,*E*)-**36**, 41436-08-2; **37**, 87696-62-6; (*E*)-**38**, 82353-28-4; (*Z*)-**38**, 82353-27-3; (*E*)-**39**, 87696-63-7; (*Z*)-**39**, 87696-64-8; (*E*)-**40**, 87696-77-3; (*Z*)-**40**, 87758-35-8; **41**, 87696-65-9; **42**, 87696-66-0; (*R**,*S**-*Z*)-**43**, 87696-67-1; (*R**,*S**-*E*)-**43**, 87696-74-0; (*R**,*R**-*Z*)-**43**, 87696-75-1; (*R**,*R**-*E*)-**43**, 87696-76-2; (*E*)-**44**, 15802-62-7; (*Z*)-**44**, 15802-63-8; **45**, 87696-68-2; **53**, 87696-72-8; $C_5H_{11}CHO$, 66-25-1; *p*-$MeOC_6H_4CHO$, 123-11-5; *p*-$NO_2C_6H_4CHO$, 555-16-8; PhCOCl, 98-88-4; Me_3CCOCl, 3282-30-2; $(CH_3)_2CO$, 67-64-1; $Me_2C(OMe)_2$, 77-76-9; *p*-$MeOC_6H_4CH(O\text{-}n\text{-}Bu)_2$, 82343-41-7; PhCHO, 100-52-7; $PhSCH_2Cl$, 7205-91-6; Me_3SiOTf, 27607-77-8; TiF_4, 7783-63-3; $FeCl_3$, 7705-08-0; $TiCl_4$, 7550-45-0; ethyl α-(diphenylmethylsilyl)acetate, 13950-57-7; ethyl α-bromoacetate, 105-36-2; diphenylmethylsilyl chloride, 144-79-6; ethyl α-(trimethylsilyl)acetate lithium enolate, 54886-62-3; 2-bromopropene, 557-93-7; β-bromostyrene, 103-64-0; (*Z*)-1-bromo-1-propene, 590-13-6; 2-bromo-2-butene, 13294-71-8; propionaldehyde, 123-38-6; tri-*n*-butyl orthoformate, 588-43-2.

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Organotin Nucleophiles. 5.[1] Palladium-Catalyzed Allylic Propargylation with Allenylstannane

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Allenyltrialkylstannanes were found to react with various allylic acetates in the presence of catalytic amounts of $Pd(PPh_3)_4$ under mild neutral conditions, providing a novel approach for obtaining the 1,5-enyne carbon skeleton. The regioselectivity of propargylation depends largely on the electron-withdrawing properties of the substituents at the two ends of the allylic system: substitution occurs at the end of closer proximity to the more electronegative group. Allylic cyanohydrin acetates are substituted at a position α to the cyano group along with formation of a reduced side product. Several mechanistic aspects of these reactions are discussed.

Allenyl metallic species of group 4A are potentially useful and interesting synthetic reagents due to their reactivities at both the allylic and vinylic positions. Although these allenyl metallic compounds are more reactive nu-

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