3600-3300, 3000-2800, 1350, 1300-1100, 1075; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.05 (d, J = 8.3 Hz, 1 H), 3.80 (d, J = 5.6 Hz, 1 H), 3.48 (d, J = 7.0 Hz, 1 H), 3.45-3.10 (m, 4 H), 2.80 (d, J = 6.7 Hz, 1 H), 2.20-1.65 (series of m, 12 H), 1.60-1.5 (m, 2 H), 1.32 (s, 6 H), 1.30-1.15 (m, 1 H), 1.17 (s, 3 H), 1.16 (s, 3 H); ^{13}C NMR (62 MHz, $CDCl_3$) ppm 102.64, 91.81, 80.80, 75.64, 72.07, 65.76, 57.65, 49.98, 45.62, 42.27, 40.29, 38.77, 35.33, 32.66, 31.82, 30.73, 28.28, 27.50, 26.51, 22.34,. 20.67, 19.81, 17.15; MS m/z (M^+) calcd 442.2211, obsd 442.2190; $[\alpha]^{20}_D$ +10.9° (c 0.22, $CHCl_3$).

Anal. Calcd for $C_{23}H_{38}O_4S_2$: C, 62.40; H, 8.65. Found: C, 62.48; H, 8.67.

(3′a*S*,6′*S*,7′*S*,8′*S*,8′a*R*,12′a*R*,13′a*S*)-Decahydro-8′a,14′,14′-trimethyl-2′-phenylspiro[1,3-dithiolane-2,12′-(9′*H*)-[4*H*-3a,6]methanobenzo[4,5]cyclodeca[1,2-*d*]dioxole]-7′,8′-diol Diacetate (23a). A solution of **21a** (13 mg, 2.85 × 10^{-5} mol) in pyridine (1 mL) was treated with a solution of osmium tetroxide in pyridine (0.17 mL of 0.25 g of OsO_4 per 5 mL, 1.2 equiv), stirred at room temperature overnight, and processed as described above. The significant insolubility of the diol prompted direct conversion in unpurified form to the diacetate.

The crude diol **22b** in anhydrous pyridine (0.6 mL) containing acetic anhydride (0.3 mL) and DMAP (3 crystals) was stirred under argon at room temperature overnight. The mixture was diluted with ethyl acetate (5 mL), washed in turn with water (5 mL), 0.12 N HCl (2 × 5 mL), saturated $NaHCO_3$ solution (2 × 5 mL), and brine (5 mL), and then dried and evaporated. Purification by silica gel chromatography gave **23a** (1 mg, unoptimized): IR ($CHCl_3$, cm^{-1}) 3020-2800, 1730, 1370, 1270-1150, 1095, 1050, 1025; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.40 (m, 2 H), 7.40-7.30 (m, 3 H), 5.76 (s, 1 H), 5.22 (s, 1 H), 5.19 (s, 1 H), 4.28 (d, J = 9.6 Hz, 1 H), 3.45-3.15 (m, 5 H), 2.13 (s, 3 H), 2.04 (s, 3 H), 2.50-1.00 (series of m, 13 H), 1.35 (s, 3 H), 1.26 (s, 3 H), 1.20 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.59, 169.36, 139.07, 128.93, 128.25, 126.81, 100.20, 91.82, 84.11, 74.87, 73.42, 68.41, 56.10, 50.24, 46.51, 43.12, 40.41, 38.67, 35.91, 32.96, 32.61, 30.77, 29.71, 22.38, 21.33, 20.94, 20.58, 20.48, 17.54; MS m/z (M^+) calcd 574.2423, obsd 574.2416; $[\alpha]^{20}_D$ -41.7° (c 0.35, $CHCl_3$).

(3′a*S*,6′*S*,7′*S*,8′*S*,8′a*R*,12′a*R*,13′a*S*)-Decahydro-2′,2′,8′a,14′,14′-pentamethylspiro[1,3-dithiolane-2,12′(9′*H*)-[4*H*-3a,6]methanobenzo[4,5]cyclodeca[1,2-*d*][1,3]dioxole]-7′,8′-diol Diacetate (23b). A solution of **22b** (23 mg, 5.2 × 10^{-5} mol) in dry pyridine (2 mL) containing acetic anhydride (1 mL) was stirred at room temperature under argon in the presence of DMAP (3 crystals) for 24 h. The usual workup and chromatographic purification gave **23b** (20 mg, 73%) as a white solid: mp 226-228 °C; IR ($CHCl_3$, cm^{-1}) 3030-2800, 1730, 1460, 1375, 1280-1200, 1140, 1075-1000, 955; ^{1}H NMR (300 MHz, C_6D_6) δ 5.64 (br s, 1 H), 5.51 (br s, 1 H), 4.53 (d, J = 9.4 Hz, 1 H), 2.85-2.60 (m, 5 H), 2.60-1.00 (series of m, 13 H), 1.81 (s, 3 H), 1.75 (s, 3 H), 1.60 (s, 3 H), 1.52 (s, 3 H), 1.46 (s, 3 H), 1.44 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 169.86, 168.67, 103.11, 92.04, 81.46, 75.43, 73.77, 68.75, 56.47, 50.81, 46.74, 43.65, 40.37, 39.01, 35.74, 33.26, 32.21, 30.90, 28.24, 27.82, 26.88, 22.92, 20.99, 20.92, 20.48, 20.42, 18.18; MS m/z (M^+) calcd 526.2323, obsd 526.2364; $[\alpha]^{20}_D$ -17.5° (c 0.2, $CHCl_3$).

Anal. Calcd for $C_{27}H_{42}O_6S_2$: C, 61.57; H, 8.04. Found: C, 61.75; H, 8.24.

Deuterium Labeling Studies. The preparations of **25-27** were carried out along lines entirely parallel to those outlined above. The chemical shift effects and NOE data of greatest relevance are provided in the illustrated formulas.

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Supplementary Material Available: Tables of X-ray crystal data, bond distances and angles, final fractional coordinates, and thermal parameters for **11** as well as the 300-MHz ^{1}H NMR spectra of those compounds for which elemental analyses are not available (11 pages). Ordering information is given on any current masthead page.

(*Z*)-α-(Trimethylsilyl) α,β-Unsaturated Esters. Their Stereoselective Conversion into α,β- and β,γ-Unsaturated Esters and β,γ-Unsaturated Ketene Acetals

M. Ramin Najafi, Mei-Ling Wang, and George Zweifel*

Department of Chemistry, University of California, Davis, California 95616

Received September 6, 1990

Deprotonation of methyl (*Z*)-α-(trimethylsilyl) α,β-unsaturated esters with lithium diisopropylamide (LDA) or with lithium hexamethyldisilazide (LHMDS) in the presence of hexamethylphosphoramide (HMPA) as an activator, followed by protonation of the intermediate dienolates with methanol, produces stereoselectively the desilylated (*E*)-3-alkenoic esters. Trapping the dienolates with chlorotrimethylsilane instead of methanol and then treatment of the resultant ketene acetals with aqueous hydrochloric acid affords (*E*)-α-(trimethylsilyl)-β,γ-alkenoic esters in 98% isomeric purities. In the absence of HMPA, (*Z*)-α-(trimethylsilyl)-α,β-alkenoic esters undergo a Michael-type addition with LDA to furnish, after methanol-mediated elimination of the diisopropylamine moiety, (*E*)-α-(trimethylsilyl)-α,β-alkenoic esters. In contrast to the behavior with the corresponding *Z* esters, deprotonation of the *E* esters with LDA does not require an activator. Treatment of the dienolate intermediates formed with chlorotrimethylsilane yields *O*-methyl-*C*,*O*-bis(trimethylsilyl)ketene acetals, and alkylation furnishes (*E*)-α-alkyl β,γ-unsaturated esters. Protodesilylation of the latter compounds with tetra-*n*-butylammonium fluoride followed by hydrolytic workup provides trisubstituted 2-alkenoates.

The protonative deconjugation of α,β-unsaturated esters has been extensively investigated and represents an important method for preparing stereodefined β,γ-unsaturated esters.[1] It thus occurred to us that subjecting the

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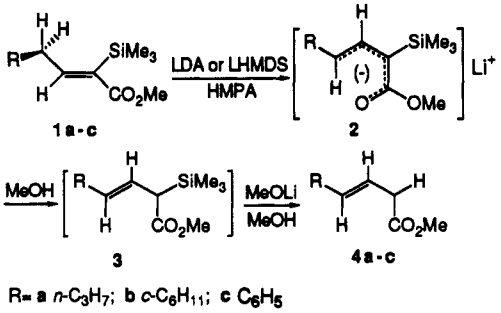
readily accessible (Z)-α-silyl α,β-unsaturated esters 1[2] to a sequence of deprotonation–protonation reactions might provide a convenient route to the α-silyl β,γ-unsaturated esters 3. These contain the synthetically exploitable and

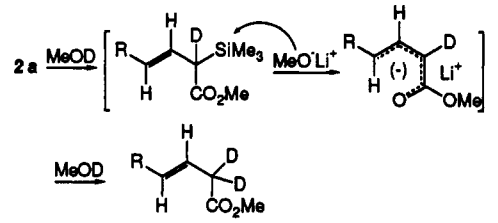
versatile allylsilyl and alkoxycarbonyl moieties and hence should be amenable to a variety of interesting synthetic transformations.[3] Although methods for preparing the esters 3 have been reported,[4,5] a general, stereoselective, and high-yield method for their synthesis is lacking. In this paper, we report the results of a study of deprotonation of (Z)-α-silyl esters 1 under various conditions and the conversion of the resultant dienolates into a variety of synthetically attractive intermediates.

In a preliminary experiment, the (Z)-α-silyl ester **1a** was added to a solution of LDA (lithium diisopropylamide, 1.1 equiv) in THF containing HMPA (hexamethylphosphoramide, 3 equiv) at −78 °C. Protonation with methanol at −78 °C followed by pouring the reaction mixture into aqueous ammonium chloride and workup, however, did not provide the β,γ-unsaturated silyl ester **3a**, but instead the corresponding desilylated *E* ester **4a** in 98% isomeric purity.[6] Under similar experimental conditions, the ester **1c** also furnished, after protonative deconjugation, the ester **4c**. However, deprotonation of the cyclohexyl-substituted ester **1b** did not proceed to completion unless lithium hexamethyldisilazide (LHMDS) in HMPA was used.[7]



R= **a** *n*-C_3H_7; **b** *c*-C_6H_{11}; **c** C_6H_5

Previous investigators have shown that kinetically controlled deprotonation of (*E*)-2-alkenoates with LDA–HMPA followed by protonation of the resultant dienolates affords the corresponding (*Z*)-3-alkenoates.[1] The observed inversion of stereochemistry was rationalized in terms of deprotonation occurring from a conformation that leads directly to the minimum energy carbanion.[1d,e] The stereoselective conversion of the ester **1**, in which the alkyl and CO_2Me substituents are also in a trans relationship, into the trans ester **4** may be rationalized similarly, but with the alkyl-$SiMe_3$ rather than the alkyl-CO_2R' steric interactions dictating the stereochemical outcome of the reaction. Thus, deprotonation of the *Z* esters **1** with LDA–HMPA or with LHMDS–HMPA from a conformation in which the R and the Me_3Si groups are anti leads to the dienolates **2**. Protonation of **2** with methanol gives **3** which is, however, susceptible to nucleophilic attack on silicon by the lithium methoxide formed in the course of the reaction to furnish the desilylated esters **4**.[8] To ascertain that formation of **4a** had indeed proceeded via an initial protonation of the dienolate **2a**, the reaction mixture was stirred with excess MeOD at −78 °C for 15 min, allowed to warm to 25 °C, maintained at this temperature for 30 min, and then poured into a mixture of saturated aqueous ammonium chloride–*n*-pentane–ice. ^1H NMR examination of the resulting β,γ-unsaturated ester revealed incorporation of 1.8 deuteriums (±0.05 D) at the C-2 carbon. Hence initial protonation of **2a** with MeOD must have occurred chemoselectively at the α-position followed by desilylation of the intermediate monodeuterated ester by the MeOLi formed.[8] Deuteration of the resultant monodeuterated dienolate furnished the dideuterated β,γ-unsaturated ester.



In an attempt to avoid the loss of the trimethylsilyl moiety at C-2 in **3**, the dienolates **2** derived from **1a–c** were trapped at −78 °C with chlorotrimethylsilane, a reaction which does not form lithium methoxide. Although isolation of the unsaturated ketene acetals **5** formed by aqueous workup resulted in considerable desilylation, hydrolysis of the crude silyl ketene acetals **5** with aqueous 5% HCl

(1) For the preparation of β,γ-unsaturated esters via deconjugative protonation of dienolates derived from *E* and *Z* α,β-unsaturated esters, see: (a) Rathke, M. W.; Sullivan, D. *Tetrahedron Lett.* **1972**, 4249. (b) Hermann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433. (c) Hase, T. A.; Kukkola, P. *Synth. Commun.* **1980**, *10*, 451. (d) Krebs. E.-P. *Helv. Chim. Acta* **1981**, *64*, 1023. (e) Kende, A.; Toder, B. H. *J. Org. Chem.* **1982**, *47*, 163. (f) Ikeda, Y.; Yamamoto, H. *Tetrahedron Lett.* **1984**, *25*, 5181. (g) Tsuboi, S.; Muranaka, K.; Sakai, T.; Takeda, A. *J. Org. Chem.* **1986**, *51*, 4944. (h) Ikeda, Y.; Ukai, L.; Ikeda, N.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 743 and references cited therein. (i) Hudlicky, T.; Fleming, A.; Radesca, L. *J. Am. Chem. Soc.* **1989**, *111*, 6691. (k) Piers, E.; Gavai, A. V. *J. Org. Chem.* **1990**, *55*, 2374.

(2) Lewis, W. Ph.D. Thesis, University of California, Davis, CA, 1979. Dansheimer, R. L.; Sard, H. *J. Org. Chem.* **1980**, *45*, 4810. Miyaura, H.; Suzuki, A. *Chem. Lett.* **1981**, 879. Cooke, M. P. *J. Org. Chem.* **1987**, *52*, 5729. Sato, Y.; Takeuchi, S. *Synthesis* **1983**, 734. For nonstereoselective syntheses of α-silyl α,β-unsaturated esters, see: Hartzell, S. L.; Rathke, M. W. *Tetrahedron Lett* **1976**, 2737. Sato, Y.; Takeuchi, S. *Synthesis* **1983**, 734.

(3) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer Verlag: Berlin, 1983. Colvin, E. *Silicon in Organic Synthesis*; Butterworths: London, 1983; Fleming, I. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 3. Magnus, P. D.; Sakar, T.; Djiuric, S. In *Comprehensive Organometallic Chemistry*; Wilkinson, G. W., Stone, F. G. A., Abel, F. W., Eds.; Pergamon: Oxford, 1982; Vol. 7.

(4) (a) Albaugh-Robertson, P.; Katzenellenbogen, J. A. *Tetrahedron Lett.* **1982**, *23*, 723. (b) Albaugh-Robertson, P.; Katzenellenbogen, J. A. *J. Org. Chem.* **1983**, *48*, 5288.

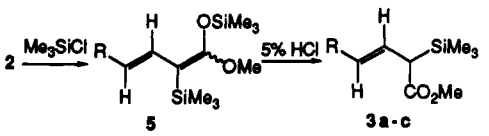
(5) Millard, A. A.; Rathke, M. W. *J. Am. Chem. Soc.* **1977**, *99*, 4833. Naruta, Y.; Uno, H.; Maruyama, K. *Chem. Lett.* **1982**, 609. Morizawa, K.; Kanemoto, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 2953. Maruyama, K.; Uno, H.; Naruta, Y. *Chem. Lett.* **1983**, 1767. Uno, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2471.

(6) The *E* esters **4a–c** could not be separated from the corresponding *Z* isomers on various silica capillary columns. Hence, the ratios of the (*E*)- and (*Z*)-3-alkenoic esters formed were determined by ^1H NMR, since the allylic protons of each pair of the isomeric esters exhibited different chemical shifts.

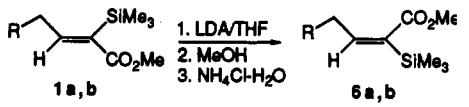
(7) Methyl (*Z*)-2-(trimethylsilyl)-3-cyclohexylpropenoate, which contains a tertiary allylic hydrogen, could not be deprotonated with LDA–HMPA under the experimental conditions used for **1**. This was evidenced by the absence of deuterium incorporation when the reaction mixture was quenched with deuterated methanol. Attempts to deprotonate the ester with LHMDS–HMPA led to a mixture of products. A similar reluctance for deprotonation has been reported for the corresponding ethyl (*E*)-3-cyclohexylpropenoate: Hase, E. T.; Kukkola, P. *Chem. Commun.* **1980**, *10*, 451.

(8) Oxygen nucleophiles such as alkoxides are known to attack α-silyl esters at silicon rather then at the α-hydrogen atoms to give the desilylated enolate ions. On the other hand, nitrogen bases such as LDA usually attack the α-hydrogen atoms to give silicon-subsituted enolates. Fleming, I. In *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 3, p 657. Brooks, A. G.; Duff, J. M.; Anderson, D. G. *J. Am. Chem. Soc.* **1970**, *92*, 7567. Chvalovsky, V. *Organomet. React.* **1972**, *3*, 191. Pandy-Szekere, D.; Deleris, G.; Picard, J.-P.; Callas, R. *Tetrahedron Lett.* **1980**, *21*, 4267.

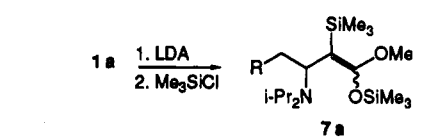
yielded the corresponding esters **3a–c** in 96–98% isomeric purities.[9,10] The trans stereochemistry of the esters is consistent with the large vicinal coupling constants (J > 15 Hz) observed for the vinylic protons in the ^{1}H NMR spectra.

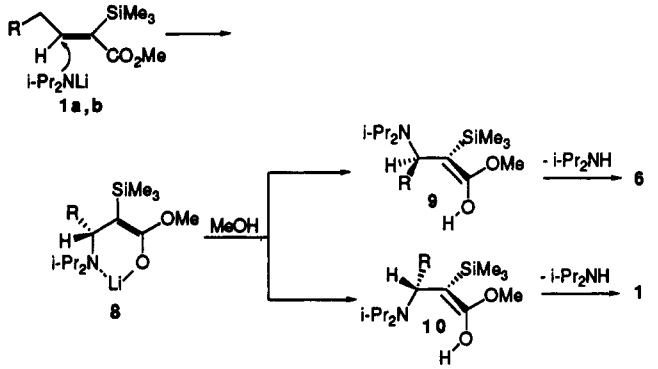


We next investigated the reaction of **1** with LDA in the absence of HMPA. It had been shown that LDA adds conjugatively to ethyl (*E*)-crotonate at −78 °C to produce, after workup, the corresponding β-amino ester in quantitative yield.[1b,c,11] Interestingly, addition of the (*Z*)-silyl esters **1a,b** to a solution of LDA (1.1 equiv) in THF at −78 °C followed by warming the reaction mixtures to 25 °C afforded, after addition of methanol at 0 °C and workup, not the corresponding β-amino esters but instead the inverted (*E*)-silyl esters **6a,b** in 98% isomeric purities.[12,13]

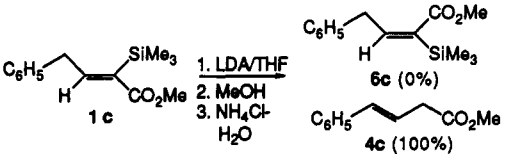


The possibility that the isomerization of the *Z* esters **1** into the corresponding *E* esters had proceeded via the intermediacy of the lithium dienolates **2** was ruled out since the *E* ester **6a** obtained by treatment of **1a** with LDA followed by quenching the reaction mixture with MeOD instead of MeOH did not result in deuterium incorporation. However, trapping the intermediate with chlorotrimethylsilane before addition of MeOH furnished the vinyl ketene acetal **7a** in 94% yield.[14] Hence, the formation of the ester **6** must have proceeded via a Michael addition of LDA to the ester **1**, followed by methanol-induced elimination of the isopropylamine moiety. The stereoselective formation of the *E* esters **6** may be rationalized as follows. Attack of LDA at C-3 of the *Z* ester **1** leads to the lithium-chelated intermediate **8** (only one enantiomer is shown). Kinetic controlled, methanol mediated elimination of *i*-Pr$_2$NH could proceed from either or both rotamers **9** and **10**. However, rotational conversion of **8** to **10** would entail eclipsing of the R and Me$_3$Si groups. Thus, the energetically more favorable elimination path should proceed via rotamer **9** to furnish the *E* ester **6**, in agreement with the experimental result.

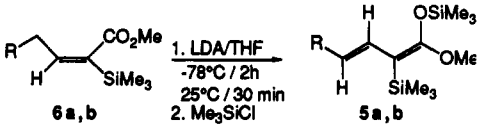




Unfortunately, treatment of the (*Z*)-phenyl-substituted ester **1c** with LDA under the experimental conditions described above did not furnish the corresponding isomerized *E* ester **6c** but instead yielded the ester **4c**. In this case the reaction may have proceeded via deprotonation of the benzylic protons by LDA rather than via conjugate addition of the base to the unsaturated ester.



Having developed an efficient synthesis of the *E* esters **6**, we next examined their reactivity toward LDA and made the interesting observation that, in contrast to the behavior of the corresponding *Z* esters **1**, the corresponding *E* esters do not require the presence of HMPA for deprotonation to occur. Thus, treatment of **6a,b** at −78 °C with a solution of LDA (1.1 equiv) in THF and maintaining the reaction mixture at this temperature for 2 h and at 25 °C for 30 min afforded the dienolate **2**. Trapping the resultant dienolates with chlorotrimethylsilane furnished the silyl ketene acetals **5a,b** in 87% and 83% yields, respectively.



The absence of HMPA in the reaction mixture made it possible to isolate compounds **5a** and **5b** by a nonaqueous workup, thus circumventing the previously observed desilylation of **5** during aqueous workup.[10] GLC analyses of compounds **5a,b** on a silica capillary column revealed only one peak, and the ^{1}H NMR spectra were consistent with a trans relationship of the vinylic protons. The tentative assignment of the *E* stereochemistry to the C1–C2 double bond is based on the reported preference for the cis relationship of the vinyl group of the alkyl-substituted double bond to the OSiMe$_3$ group in 1-ethoxy-1-(trimethylsiloxy)butadiene.[14] Moreover, the presence of the Me$_3$Si moiety at C-2 should strengthen the preference for the *E* configuration of the terminal double bond.

The observed differential behaviors of the *Z* esters **1** and the *E* esters **6** toward LDA in the absence of HMPA may be associated with the geometries of the two esters. Assuming that the reaction with LDA proceeds via an initial coordination of the ester carbonyl group with lithium,[15]

(9) It has been shown that deprotonation of an *E,Z* mixture of *tert*-butyl 2-(trimethylsilyl)-2-pentenoate with LDA followed by protonation furnishes *tert*-butyl (*E*)-2-(trimethylsilyl)-3-pentenoate.[4b]

(10) It should be noted that the presence of HMPA alone during the aqueous workup of **3** causes partial desilylation of the esters.

(11) Uyehara, T.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 753.

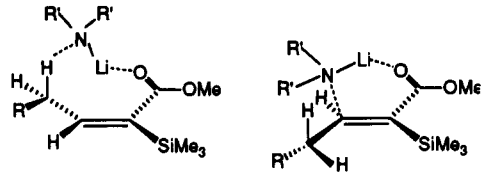
(12) It has been reported that deprotonation of ethyl (*E,E*)-4-methyl-2-(trimethylsilyl)hepta-2,4-dienoate with LDA in the absence of HMPA proceeds with loss of the trimethylsilyl moiety to furnish the corresponding deconjugated dienoic ester. Fleming, I.; Iqbal, J.; Krebs, E.-P. *Tetrahedron* **1983**, *39*, 841.

(13) Attempts to isomerize (*Z*)-*n*-C$_3$H$_7$CH$_2$CH=C(SiMe$_3$)CO$_2$H into the corresponding *E* acid in the presence of bromine and pyridine while irradiating with uv light furnished a 15:85 mixture of the isomeric acids. Zweifel, G.; On, H. P. *Synthesis* **1980**, 803. On, H. P. Ph.D. Thesis, University of California, Davis, CA 1982.

(14) We have not established the stereochemistry of the ketene acetal moiety in **5a,b** and **7**. For a discussion of the stereochemistry of silyl ester polyenolates, see: Hertler, W. R.; Reddy, G. S.; Sogah, D. Y. *J. Org. Chem.* **1988**, *53*, 3532.

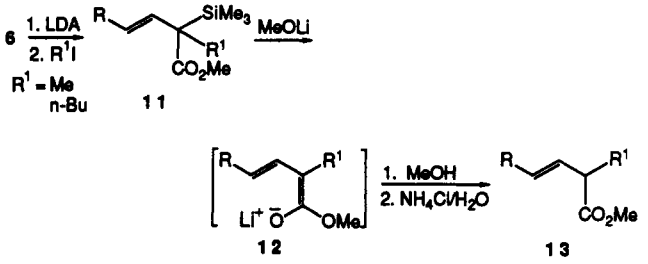
(15) Laube, T.; Dunitz, J. K.; Seebach, D. *Helv. Chim. Acta* **1985**, *65*, 1373. Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624.

abstraction of the proton via an eight-membered ring transition state[16] then is geometrically favorable for the *E* esters A to furnish a dienolate with the *E* stereochemistry at the C3–C4 double bond, while conjugate addition of LDA prevails for the *Z* ester B.



A B

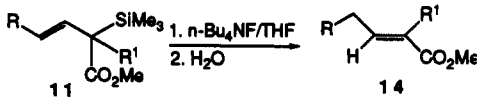
The successful conversion of the *E* esters **6** into the corresponding unsaturated ketene acetals **5** prompted us to investigate their reaction with carbon electrophiles as a procedure for preparing α-alkylated β,γ-unsaturated esters **11**. Thus, **6** was treated sequentially with LDA at −78 °C and then with methyl iodide or with *n*-butyl iodide. Workup and distillation furnished the *E* alkylated esters **11** in 96 to 99% isomeric purities. Next, we investigated the conversion of **11** into the corresponding desilylated esters **13**. Treatment of the esters **11** with a solution of lithium methoxide in methanol and aqueous workup furnished the *E* α-alkylated esters **13**. Lithium methoxide mediated desilylation of **11** followed by protonation of the resultant lithium dienolate **12** by methanol at the α-position accounts for the formation of the deconjugated ester **13**.



12 **13**

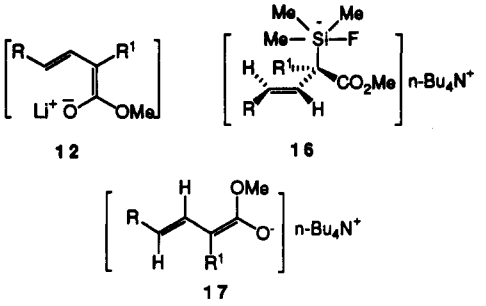
Fluoride-induced reactions of allylic silanes with electrophiles have been the object of a number of investigations.[17] Sakurai and co-workers have suggested that addition of fluoride ion to allylic silanes generates allyl anions which then react with electrophiles in a nonregioselective manner.[18] Recently, Majetich and co-workers have proposed that fluoride-induced allylations of Michael acceptors using allylic silanes proceed via the intermediacy of pentacoordinate allylic silicates.[19]

Remarkably, protodesilylation of **11** with a solution of *n*-Bu_4NF (1.1 equiv) in THF followed by hydrolytic workup yielded the *E* trisubstituted olefins **14**.[20,22] Thus, in



11 **14**

contrast to the observed α-protonation of the enolate **12** derived from desilylation of **11** with lithium methoxide, the fluoride-induced protodesilylation of the allylic silanes **11** proceeds via γ-protonation to give the conjugated esters **14**. Obviously, the dienolate ions formed from the lithium methoxide and tetra-*n*-butylammonium fluoride mediated desilylations of **11** must be of a different nature. Also, formation of the trisubstituted olefins **14** via the intermediacy of an allylic pentacoordinated organosilicon nucleophile **16**, which then undergoes protodesilylation via an S_E2' type mechanism,[23] is difficult to reconcile with the observed high *E* stereoselectivity.



12 **16**

17

It is generally accepted that lithium dienolates, derived from enoates, adopt the s-cis conformation **12** and undergo electrophilic attack under kinetic control to give products of α-substitution.[1,24] Although a firm rationalization for the observed stereoselective formation of the conjugated ester **14** via fluoride ion mediated protodesilylation cannot be advanced at present, it is conceivable that the reaction of **11** with *n*-Bu_4NF may involve the s-trans dienolate **17**, which is then protonated at the γ-position to furnish the *E* ester **14**. In this connection it is worth noting that in the presence of added LiI (1.1 equiv), the ester **11** upon treatment with a solution of *n*-Bu_4NF (1.1 equiv) in THF at 0 °C and quenching the reaction mixture with water did not afford the trisubstituted olefin **14**, but instead furnished mainly the desilylated ester **13** along with starting material. This suggests that the LiI present in the reaction mixture traps the anion formed as the lithium dienolate **12**, which then undergoes α-protonation (vide infra). Thus, the dienolate counterion plays a decisive role in determining the nature of the product formed in *n*-Bu_4NF mediated desilylations of the allylic esters **11**.

In view of the observed differential reaction patterns of the dienolates derived from the α-alkylated esters **11** with lithium methoxide and tetrabutylammonium fluoride, respectively, toward protonation, we included in our study the ester **3a**, which does not possess an α-alkyl substituent. Addition of a solution of lithium methoxide in methanol to **3a** afforded, after hydrolytic workup, the anticipated desilylated ester **4a**. However, sequential treatment of **3a** with a solution of *n*-Bu_4NF in THF followed by addition of water under conditions similar to those used for the conversion of the ester **11** into the ester **14** did not afford the α,β-unsaturated ester **18**, but instead furnished a condensation product whose distinguishing features of the ^1H NMR spectrum (300 MHz) are a triplets at 6.8 (1 H) ppm, pointing to the presence of a trisubstituted double bond; two singlets at 3.7 and 3.6 ppm (two OCH_3 groups);

(16) Eight-membered ring transition states have been suggested in certain LDA-mediated proton transfer reactions: Majewski, M.; Green, J. R.; Snieckus, V. *Tetrahedron Lett.* **1986**, *27*, 531. Wilson, S. R.; Price, M. F. *Tetrahedron Lett.* **1983**, 569.

(17) Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. A.; Vyazankin, N. S. *Tetrahedron* **1988**, *44*, 2675.

(18) Hosomi, A.; Shirhata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 3043. Sakurai, H. *Synthesis* **1989**, 1.

(19) Majetich, G.; Casares, A.; Chapman, D.; Behnke, M. *J. Org. Chem.* **1986**, *51*, 1745. Majetich, G.; Desmond, R. W.; Soria, J. J. *J. Org. Chem.* **1986**, *51*, 1753.

(20) The *E* stereochemistry of **13** follows from NOE experiments and from the fact that the vinylic protons of trisubstituted (*E*)-2-alkenoic esters absorb at 6.7 ppm while the corresponding *Z* isomers absorb at 5.9 ppm.[21]

(21) Chan, K. C.; Jewell, R. A.; Nutting, W. H.; Rapoport, H. *J. Org. Chem.* **1968**, *33*, 3382.

(22) Interestingly, treatment of a mixture of **11** and water (12 equiv) with a solution of *n*-Bu_4NF in THF yielded, after aqueous workup, exclusively the ester **13**.

(23) Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281.

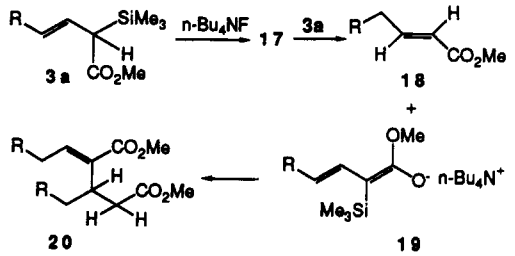
(24) Yamamoto, Y.; Hatsuya, S.; Yamada, J. *J. Org. Chem.* **1990**, *55*, 3118 and references cited therein.

Table I. Yields of Unsaturated Esters and Unsaturated Ketene Acetals

product	R	yield,%[a,b]	product	R	R^1	yield,%[a,b]
1a	n-C_3H_7	69(98)[c]	6b	c-C_6H_{11}		78(98)
1b	c-C_6H_{11}	64(98)[c]	11-1	n-C_3H_7	CH_3	89(99)
1c	C_6H_5	55(98)[c]	11-2	n-C_3H_7	n-C_4H_9	85(96)
3a	n-C_3H_7	71(98)	11-3	c-C_6H_{11}	CH_3	82(98)
3b	c-C_6H_{11}	84(98)	11-4	c-C_6H_{11}	n-C_4H_9	71(98)
3c	C_6H_5	88(94)	13-1	n-C_3H_7	CH_3	83(99)
4a	n-C_3H_7	77(97)[d]	13-2	n-C_3H_7	n-C_4H_9	81(96)
4b	c-C_6H_{11}	96(96)[d]	13-4	c-C_6H_{11}	n-C_4H_9	80(99)
4c	C_6H_5	81(96)[d]	14-1	n-C_3H_7	CH_3	75(97)
5a	n-C_3H_7	87	14-2	n-C_3H_7	n-C_4H_9	74(94)
5b	c-C_6H_{11}	83	14-4	c-C_6H_{11}	n-C_4H_9	84(97)
6a	n-C_3H_7	86(98)				

[a] Isolated yields. Isomeric purities are in parentheses. [b] The IR, ^1H NMR, ^{13}C NMR, and mass spectral data of the compounds were consistent with the assigned structures. [c] Yields are based on 1-(trimethylsilyl)-1-alkynes. [d] Reference 6.

a multiplet at 3.1 (1 H) ppm; two doublets of doublets at 2.7 and 2.6 (1 H each) ppm, indicating the presence of a CH_2 group adjacent to a prochiral center, and two triplets at 0.9 and 0.8 (two CH_3 groups) ppm. Both the ^1H NMR and ^{13}C NMR data suggest that the main component of the mixture possesses the structure **20**. The assignment of the *E* configuration to the major compound is based on the observation that a vinylic proton cis to an ester group generally absorbs at ~6.7 ppm, whereas a proton trans to the ester group absorbs at ~5.9 ppm.[21] The NMR spectra showed some additional absorptions due to minor impurities, which were confirmed by GLC analysis of the reaction mixture on various silica capillary columns.



Although the nature of intermediates leading to the condensation product **20** remains to be established, its formation may be envisioned to proceed via an initial attack of F^- on silicon of **3a** to give a dienolate **17** (R^1 = H). Protonation of the dienolate **17** by **3a** leads to the conjugated ester **18** and the dienolate **19**, which may be the precursors for diester **20**. The driving force for this condensation reaction is the facility for deprotonation of the α-hydrogen of **3a** by **17**, imparted by the CO_2Me, $SiMe_3$ groups and the adjacent double bond. Thus, it is clear why the reaction of ester **11**, which does not possess an α-hydrogen, with tetrabutylammonium fluoride cannot lead to condensation but stops at the desilylation step to give upon workup the conjugated ester **14**.

In conclusion, our investigations have uncovered novel and operationally convenient procedures for stereoselective conversions of the readily accessible (*Z*)-α-silyl α,β-unsaturated esters **1** into the synthetically valuable α-silyl β,γ-unsaturated esters **3**, (*E*)-β,γ-unsaturated esters **4**, and (*E*)-α-silyl α,β-unsaturated esters **6**. Moreover, deprotonation of (*E*)-α-silyl α,β-unsaturated esters **6** with LDA and trapping the resultant dienolates with chlorotrimethylsilane provides a novel approach for the preparation of β,γ-unsaturated *C,O*-bis(trimethylsilyl)ketene acetals **5**. Finally, the stereoselective preparation of trisubstituted esters **14** from readily accessible precursors is of special importance in that many biogenetically interesting isoprenoid molecules and insect pheromones embody trisubstituted olefinic moieties. A summary of the results obtained in this study is shown in Table I.

Experimental Section

Ether and tetrahydrofuran were distilled from sodium and benzophenone immediately prior to use. Hexamethylphosphoramide (HMPA) and diisopropylamine were distilled from crushed calcium hydride prior to use. 1-(Trimethylsilyl)-1-hexyne[25] and 1-(trimethylsilyl)-3-cyclohexyl-1-propyne[26] were prepared according to the literature. Tetra-*n*-butylammonium fluoride (Aldrich, 1.0 M solution in THF, <5% H_2O) was stored over 4-Å molecular sieves. The glassware for reactions involving organometallic reagents was oven-dried at 150 °C for 6 h, assembled hot, and cooled under a stream of nitrogen before use. All reactions involving these reagents were stirred magnetically and conducted under an atmosphere of nitrogen. ^1H NMR spectra were recorded at 300 MHz using $CDCl_3$ as the solvent with the residual $CHCl_3$ therein serving as the internal standard. ^{13}C NMR spectra were recorded at 75.5 MHz and are referenced to the central triplet peak of $CDCl_3$ at 77.00 ppm. The purities of the products obtained were determined by GC on fused silica capillary (J&W) columns. Elemental analyses were performed by the Microanalytical Laboratory, University of California, Berkeley, CA.

Methyl (*Z*)-2-(Trimethylsilyl)-2-heptenoate (1a). Into a dry two-neck flask equipped with a magnetic stirrer, a thermometer, and a Friedrich condenser were placed 1-(trimethylsilyl)-1-hexyne (6.2 g, 40 mmol) and ether (20 mL). To this was added at 25–35 °C (water bath) neat Dibal-H (7.8 mL, 42 mmol). The mixture was warmed to 40 °C and stirred for 2 h. The ether was removed (high vacuum) and replaced by *n*-heptane (20 mL). A slow stream of dry carbon dioxide was introduced into the reaction mixture at 0 °C for 30 min and then at 60 °C for 3 h. To avoid evaporation of the solvent, ice–water was circulated through the condenser. The mixture was transferred via a double-ended needle into a vigorously stirring mixture of 10% HCl (40 mL), ether (40 mL), and crushed ice (~40 g). Vigorous stirring was continued for an additional 15 min. The phases were separated, and the aqueous phase was extracted with ether. The combined organic phases were washed with 10% HCl (2 × 20 mL), H_2O (20 mL), and brine (2 × 20 mL) and dried ($MgSO_4$). Distillation (short path) of the residue gave 5.8 g (73%) of the (*Z*)-2-(trimethylsilyl)-2-heptenoic acid: bp 90 °C (0.1 mmHg); n^{25}_D 1.4676; IR (neat) 3400–2700 (CO_2H), 1660 (C=O), 1595 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (s, 9 H, $SiMe_3$), 0.90 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.41 (m, 4 H, CH_2), 2.30 (m, 2 H, CH_2C=C), 7.30 (t, *J* = 7.5 Hz, 1 H, CH=C), 11.86 (bs, 1 H, CO_2H); ^{13}C NMR ($CDCl_3$) δ 0.65, 13.88, 22.41, 31.17, 31.38, 133.19, 159.97, 176.95. Examination of the carboxylic acid by NMR showed that it was 96% isomerically pure.

The carboxylic acid was esterified as follows. Into a 50-mL two-neck flask equipped with a Friedrich condenser were placed the crude (undistilled) (*Z*)-2-(trimethylsilyl)-2-heptenoic acid (15 g, 74 mmol) and dry methanol (30 mL, 740 mmol). To this mixture was added at room temperature freshly distilled BF_3·OEt_2 (9.1 mL, 74 mmol). The mixture was refluxed (60–70 °C) for 16 h, cooled to room temperature, and then quenched with a 10%

(25) Zweifel, G.; Lewis, W. *J. Org. Chem.* **1978**, *43*, 2739.
(26) Rajagopalan, S.; Zweifel, G. *Synthesis* **1984**, 111 (ref 7).

solution of Na_2CO_3 (75 mL). The organic phase was separated, the aqueous phase was extracted with pentane (2 × 40 mL), and the combined organic phases were washed with H_2O (20 mL), brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) of the residue afforded 12.2 g (95%) of **1a**: bp 68 °C (1 mmHg); n^{25}_D 1.4536; IR (neat) 1700 (C=O), 1600 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.19 (s, 9 H, $SiMe_3$), 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 1.32 (m, 4 H, CH_2), 2.22 (m, 2 H, CH_2C=C), 3.67 (s, 3 H, OCH_3), 7.11 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 0.55, 13.88, 22.40, 31.25, 31.34, 51.30, 133.97, 157.18, 171.87. Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.92; H, 10.60. GLC examination (30-m SE-54 silica capillary column, 140 °C) revealed that the ester was 98% isomerically pure.

Methyl (Z)-2-(Trimethylsilyl)-4-cyclohexyl-2-butenoate (1b). Following the procedure for the preparation of **1a**, 1-(trimethylsilyl)-3-cyclohexyl-1-propyne (11 g, 58 mmol) was converted in 60% yield to the (Z)-2-(trimethylsilyl)-4-cyclohexyl-2-butenoic acid. An aliquot of the acid was distilled (Kugelrohr): bp 120 °C (10^{-3} mmHg); n^{25}_D 1.4946; IR (neat) 3400–2700 (CO_2H), 1660 (C=O), 1600 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (s, 9 H, $SiMe_3$), 0.90–1.74 (m, 11 H, cyclohexyl), 2.20 (t, J = 7.5 Hz, 2 H, CH_2C=C), 7.38 (t, J = 7.5 Hz, 1 H, CH=C), 12.30 (bs, 1 H, CO_2H); ^{13}C NMR ($CDCl_3$) δ 0.78, 26.26, 26.33, 33.23, 38.22, 39.17, 133.70, 159.22, 177.26. The remaining crude acid was converted to the ester **1b** as described above. Distillation (Kugelrohr) gave 9.3 g (64%) (overall yield from silyl acetylene) of **1b**: bp 94 °C (0.05 mmHg); n^{24}_D 1.5048; IR (neat) 1700 (C=O), 1600 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.20 (s, 9 H, $SiMe_3$), 0.8–1.80 (m, 11 H, cyclohexyl), 2.14 (t, J = 7.5 Hz, 2 H, CH_2C=C), 3.68 (s, 3 H, OCH_3), 7.15 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 0.68, 26.26, 26.35, 33.22, 38.20, 39.18, 51.32, 134.47, 156.32, 171.90; high-resolution MS m/z 239.1460 (calcd for $C_{14}H_{26}O_2Si$ 239.1467). GC examination (30-m SE-54 silica capillary column, 170 °C) revealed that **1b** was 98% isomerically pure.

1-(Trimethylsilyl)-3-phenyl-1-propyne. To a solution of 3-phenyl-1-propyne (1.2 g, 10 mmol) in THF (10 mL) was added at −50 °C (33% aqueous $CaCl_2$/dry ice bath) a 1.36 M solution of MeLi (7.7 mL, 11 mmol) in ether. This reaction mixture was stirred at −50 °C for 1.5 h, treated with chlorotrimethylsilane (1.3 g, 12 mmol), stirred for 10 min, warmed to room temperature, stirred for 2 h, and then poured into a separatory funnel containing pentane (80 mL), a saturated solution of NH_4Cl (80 mL), and crushed ice (~80 g). The organic layer was separated, and the aqueous phase was extracted with pentane (2 × 50 mL). The combined pentane extracts were washed with 5% HCl (2 × 50 mL) and brine (2 × 50 mL) and dried over $MgSO_4$. Concentration and distillation (Kugelrohr) afforded 1.6 g (84%) of 1-(trimethylsilyl)-3-phenyl-1-propyne: bp 70–75 °C (1 mmHg); n^{23}_D 1.5066; IR (neat) 2180 (C≡C), 1250, 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (s, 9 H, $SiMe_3$), 3.58 (s, 2 H, CH_2), 7.10–7.30 (m, 5 H, phenyl); ^{13}C NMR ($CDCl_3$) δ 0.09, 26.14, 86.83, 104.30, 126.52, 127.82, 128.43, 136.36. The purity of the compound by GC (30-m SE-54 silica capillary column, 160 °C) was 92%.

Methyl (Z)-2-(Trimethylsilyl)-4-phenyl-2-butenoate (1c). Into a two-neck flask equipped with a magnetic stirrer, a thermometer, and a Friedrich condenser was placed 1-(trimethylsilyl)-3-phenyl-1-propyne (0.64 g, 3.4 mmol) in ether (2 mL) and neat Dibal-H (0.68 mL, 3.8 mmol) was added at 25–35 °C (water bath). The mixture was warmed to 40 °C and stirred for 2 h. The ether was removed (high vacuum) and replaced by n-heptane (2 mL). The reaction mixture was cooled to 0 °C, treated with a 1.35 M solution of MeLi (2.8 mL, 3.8 mmol), warmed to room temperature, and stirred for 15 min. A slow stream of dry carbon dioxide was introduced into the reaction mixture at 0 °C for 30 min and then at 60 °C for 3 h. To avoid evaporation of the solvent, ice–water was circulated through the condenser. The mixture was transferred via a double-ended needle into a vigorously stirring mixture of 10% HCl (5 mL), ether (5 mL), and crushed ice (~5 g). Vigorous stirring was continued for an additional 15 min. The phases were separated, and the aqueous phase was extracted with ether. The combined organic phases were washed with 10% HCl (2 × 5 mL), H_2O (5 mL), and brine (2 × 5 mL) and dried ($MgSO_4$). Recrystallization of the residue from n-hexane gave 0.54 g (68%) of the (Z)-2-(trimethylsilyl)-4-phenyl-2-butenoic acid: mp 72–74 °C (760 mmHg); IR (neat) 3400–2700 (CO_2H), 1660 (C=O), 1595 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.31 (s, 9 H, $SiMe_3$), 3.65 (d, J = 7.5 Hz, 2 H, CH_2C=C), 7.11–7.44 (m, 6 H, phenyl H's and CH=C-CO_2); ^{13}C NMR ($CDCl_3$) δ 0.75, 37.61, 126.57, 128.49, 128.72, 134.27, 138.50, 156.97, 176.95. Examination of the carboxylic acid by NMR showed that it was 98% isomerically pure.

The carboxylic acid was esterified as follows. Into a dry 25-mL two-neck flask equipped with a Friedrich condenser were placed (Z)-2-(trimethylsilyl)-4-phenyl-2-butenoic acid (0.23 g, 1.0 mmol), anhydrous K_2CO_3 (0.21 g, 1.5 mmol), dry acetone (6.5 mL) and dry MeI (1 mL). The reaction mixture was warmed to 50 °C and stirred for 90 min. During the coming 3 h, MeI (1 mL) was added every 90-min interval. After the last addition of MeI, the reaction slurry was stirred for 90 min and cooled to room temperature. The solvent was removed by high vacuum and replaced by pentane (15 mL) and a 10% solution of K_2CO_3 (10 mL). The organic phase was separated, the aqueous phase was extracted with pentane (2 × 15 mL), and the combined organic phases were washed with brine (2 × 15 mL), dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) of the residue afforded 0.20 g (81%) of **1c**: bp 80–82 °C (0.01 mmHg); n^{25}_D 1.5165; IR (neat) 1700 (C=O), 1600 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.36 (s, 9 H, $SiMe_3$), 3.70 (d, J = 7.2 Hz, 2 H, CH_2C=C), 3.76 (s, 3 H, OCH_3), 7.20–7.42 (m, 6 H, phenyl H's and CH=CCO_2); ^{13}C NMR ($CDCl_3$) δ 0.55, 37.49, 51.28, 126.38, 128.36, 128.55, 135.00, 138.62, 154.05, 171.33; high-resolution MS m/z 248.1245 (calcd for $C_{14}H_{20}O_2Si$ 248.1233). GC examination (30-m DB-210 silica capillary column, 170 °C) revealed that the ester was 98% isomerically pure.

Methyl (E)-2-(Trimethylsilyl)-3-heptenoate (3a). A solution of freshly distilled diisopropylamine (0.22 g, 2.2 mmol) in THF (4 mL) at −78 °C was treated with a 1.6 M solution of n-BuLi (1.4 mL, 2.2 mmol) in n-hexane. The mixture was stirred at −78 °C for 15 min, allowed to warm to 0 °C, stirred for an additional 15 min at 0 °C, brought to −78 °C, and then was treated with HMPA (1.2 mL, 6.6 mmol). The slurry formed was warmed to 0 °C, stirred for 10 min, cooled to −78 °C, and treated with **1a** (0.43 g, 2.0 mmol). The resulting light yellowish mixture was stirred at −78 °C for 2 h, treated with freshly distilled Me_3SiCl (0.30 mL, 2.4 mmol), stirred at −78 °C for 30 min, and then was quenched by pouring it into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). This procedure removed the HMPA without appreciable hydrolysis of the intermediate vinylketene acetal. The phases were separated, and the organic layer was stirred vigorously with 5% HCl (20 mL) for 15 min in an Erlenmeyer flask to hydrolyze the ketene acetal. The phases were separated, and the organic phase was washed with brine, dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) gave 0.30 g (71%) of **3a**: bp 60 °C (1 mmHg); n^{23}_D 1.4452; IR (neat) 1710 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.04 (s, 9 H, $SiMe_3$), 0.78 (t, J = 7.5 Hz, 3 H, CH_3), 1.28 (m, 2 H, CH_2), 1.88 (m, 2 H, CH_2), 2.74 (d, J = 10.2 Hz, 1 H, $CHCO_2$), 3.53 (s, 3 H, OCH_3), 5.19 (dt, J = 15.3, 6.9 Hz, 1 H, CH=$CCCO_2$), 5.51 (ddt, J = 15.3, 10.2, 0.9 Hz, 1 H, C=$CHCCO_2$); ^{13}C NMR ($CDCl_3$) δ −3.1, 13.7, 22.7, 34.6, 43.2, 50.8, 124.4, 129.5, 173.6. No ^{13}C NMR signals assignable to the stereoisomer were detected. Anal. Calcd. for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.61; H, 10.57. GC analysis (30-m SE-54 silica capillary column, 140 °C) of the distillate revealed that **3a** was at least 98% isomerically pure.

Methyl (E)-2-(Trimethylsilyl)-4-cyclohexyl-3-butenoate (3b). A solution of freshly distilled hexamethyldisilazane (0.36 g, 2.2 mmol) in THF (4 mL) at −78 °C was treated with a 1.6 M solution of n-BuLi (1.4 mL, 2.2 mmol) in n-hexane. The reaction mixture was stirred at −78 °C for 15 min, allowed to warm to 0 °C, stirred for an additional 15 min, brought to −78 °C, and then treated with HMPA (1.2 mL, 6.6 mmol). The slurry formed was warmed to 0 °C, stirred for 10 min, cooled to −78 °C, and treated with **1b** (0.51 g, 2.0 mmol). The mixture was stirred at −78 °C for 30 min, treated with freshly distilled Me_3SiCl (0.30 mL, 2.4 mmol), stirred at −78 °C for 30 min, and then was quenched by pouring it into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The phases were separated, and the organic layer was stirred vigorously with 5% HCl (20 mL) for 15 min to hydrolyze the ketene acetal. The organic phase was washed with brine, dried

($MgSO_4$), concentrated, and distilled (Kugelrohr) to give 0.31 g (84%) of **3b**: bp 80 °C (10^{-2} mmHg); n^{25}_D 1.4712; IR (neat) 1710 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66 (s, 9 H, $SiMe_3$), 1.0–2.0 (m, 11 H, cyclohexyl), 2.82 (d, J = 9.9 Hz, 1 H, $CHCO_2$), 3.65 (s, 3 H, OCH_3), 5.26 (dd, J = 15.6, 6.9 Hz, 1 H, CH=$CCCO_2$), 5.58 (ddd, J = 15.6, 9.9, 0.9 Hz, 1 H, C=$CHCCO_2$); ^{13}C NMR ($CDCl_3$) δ -2.88, 26.03, 26.17, 33.20, 33.37, 40.88, 43.42, 51.04, 92.74, 121.77, 135.83, 173.96. No ^{13}C NMR signals assignable to the *Z* isomer were detected. High-resolution MS m/z 254.1694 (calcd for $C_{14}H_{26}O_2Si$ 254.1702). GC analysis (50-m DB-1701 silica capillary column, 130 °C) of the distillate revealed that the product was 98% isomerically pure.

Methyl (*E*)-2-(Trimethylsilyl)-4-phenyl-3-butenoate (3c). Following the procedure for the preparation of **3a**, the ester **1c** (0.50 g, 2.0 mmol) was added dropwise to a mixture of LDA (2.2 mmol) and HMPA (6.6 mmol). The resulting dienolate was then treated with freshly distilled trimethylsilyl chloride (0.30 mL, 2.4 mmol). Workup and distillation (Kugelrohr) furnished 0.44 g (88%) of **3c**: bp 85 °C (10^{-3} mmHg); n^{24}_D 1.5246; IR (neat) 1710 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.14 (s, 9 H, $SiMe_3$), 3.10 (d, J = 9.9 Hz, 1 H, $CH\text{-}CO_2$), 3.70 (s, 3 H, OCH_3), 6.25 (d, J = 16.2 Hz, 1 H, CH=$CCCO_2$), 6.47 (dd, J = 16.2, 9.9 Hz, 1 H, C=$CHCCO_2$), 7.30 (m, 5 H, phenyl H's); ^{13}C NMR ($CDCl_3$) δ -2.79, 44.33, 51.15, 125.24, 125.86, 126.81, 128.43, 128.58, 137.52, 173.23; high-resolution MS m/z 248.1214 (calcd for $C_{14}H_{20}O_2Si$ 248.1232). GC analysis (30-m DB-1701 silica capillary column, 150 °C) of the distillate revealed 94% of **3c** and 6% of the desilylated product **4c**.

Methyl (*E*)-3-Heptenoate (4a). To a solution of freshly distilled diisopropylamine (0.22 g, 2.2 mmol) in THF (4 mL), cooled to -78 °C, was added a 1.6 M solution of *n*-BuLi (1.4 mL, 2.2 mmol) in *n*-hexane. The mixture was stirred at -78 °C for 15 min, allowed to warm to 0 °C, stirred for an additional 15 min, brought to -78 °C, and treated with HMPA (1.2 mL, 6.6 mmol). The slurry was warmed to 0 °C, stirred for 10 min, cooled to -78 °C, and treated with **1a** (0.43 g, 2.0 mmol). The light yellowish mixture was stirred for 2 h, quenched at -78 °C with MeOH (1 mL), stirred at -78 °C for 15 min, and then was poured into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The phases were separated, and the organic phase was washed with 5% HCl (2 × 10 mL), brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) afforded 0.22 g (77%) of **4a**: bp 50 °C (2 mmHg); n^{25}_D 1.4307; IR (neat) 1725 (C=O), 970 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 1.35 (m, 2 H, CH_2CH_3), 1.97 (m, 2 H, CH_2C=C), 3.00 (d, J = 5.1 Hz, 2 H, CH_2CO_2), 3.65 (s, 3 H, OCH_3), 5.50 (m, 2 H, HC=CH); ^{13}C NMR ($CDCl_3$) δ 13.59, 22.29, 34.53, 37.93, 51.69, 121.59, 134.70, 172.60. No ^{13}C NMR signals assignable to the stereoisomer were detected. Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.55; H, 10.04. GC analysis (30-m SE-54 glass capillary column, 150 °C) revealed 98% **4a** and 2% **6a**. Integration of the allylic protons absorptions in ^1H NMR spectrum showed that the compound was 97% isomerically pure.

Methyl (*E*)-4-Cyclohexyl-3-butenoate (4b). To a solution of freshly distilled hexamethyldisilazane (0.36 g, 2.2 mmol) in THF (4 mL), cooled to -78 °C, was added a 1.6 M solution of *n*-BuLi (1.4 mL, 2.2 mmol) in *n*-hexane. The mixture was stirred at -78 °C for 15 min, allowed to warm to 0 °C, stirred for an additional 15 min at 0 °C, brought to -78 °C, and treated with HMPA (1.2 mL, 6.6 mmol). The resulting yellow slurry was warmed to 0 °C, stirred for 10 min, cooled to -78 °C, and treated with **1b** (0.51 g, 2.0 mmol). The mixture was stirred for 2 h at -78 °C, quenched with MeOH (1 mL) at -78 °C, stirred at -78 °C for 15 min, and poured into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The phases were separated, and the organic phase was washed with 5% HCl (3 × 10 mL) and brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) yielded 0.35 g (96%) of **4b**: bp 85–90 °C (3 mmHg); n^{25}_D 1.4661; IR (neat) 1725 (C=O), 970 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0–2.0 (m, 11 H, cyclohexyl), 2.99 (dd, J = 4.5, 0.9 Hz, 2 H, CH_2CO_2), 3.64 (s, 3 H, OCH_3), 5.45 (m, 2 H, CH=CH); ^{13}C NMR ($CDCl_3$) δ 25.91, 26.07, 32.71, 37.91, 40.50, 51.55, 118.99, 140.46, 172.51. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.29; H, 9.83. The purity of the ester by GC (30-m DB-1701 silica capillary column, 130 °C) was 96%.

Methyl (*E*)-4-Phenyl-3-butenoate (4c). Following the procedure for the preparation of **4a**, the ester **1c** (0.75 g, 3.0 mmol) was converted to **4c**: 0.43 g (81%); bp 80 °C (0.3 mmHg, Kugelrohr); n^{27}_D 1.5392; IR (neat) 1725 (C=O), 960 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.27 (dd, J = 7.2, 1.2 Hz, 2 H, CH_2C=C), 3.74 (s, 3 H, OCH_3), 6.23 (dt, J = 15.9, 7.2 Hz, 1 H, C=$CHCCO_2$), 6.50 (d, J = 15.9 Hz, 1 H, CH=$CCCO_2$), 7.33 (m, 5 H, phenyl H's); ^{13}C NMR ($CDCl_3$) δ 38.19, 51.86, 121.63, 126.26, 127.52, 128.49, 133.46, 136.80, 171.92; high-resolution MS m/z 176.0832 (calcd for $C_{11}H_{12}O_2$ 176.0837). The purity of the ester by GC (30-m DB-1701 silica capillary column, 150 °C) was 96%.

Methyl (*E*)-2-(Trimethylsilyl)-2-heptenoate (6a). To a solution of freshly distilled diisopropylamine (0.22 g, 2.2 mmol) in THF (4 mL) at -78 °C was added a 1.6 M solution of *n*-BuLi (1.4 mL, 2.2 mmol) in *n*-hexane. The mixture was stirred at -78 °C for 15 min, allowed to warm to 0 °C, stirred for an additional 15 min at 0 °C, brought to -78 °C, treated with **1a** (0.43 g, 2.0 mmol), and stirred at -78 °C for 2 h. The resulting light yellow solution was gradually warmed to room temperature (23 °C), stirred for an additional 10–15 min, quenched with MeOH (1 mL) at 0–5 °C (ice bath), and then was poured into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The phases were separated, the organic phase was washed with 5% HCl (2 × 10 mL) and brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. GLC analysis of the residue before distillation (30-m SE-54 glass capillary column, 150 °C) indicated a 98:2 mixture of the *E* and *Z* isomeric esters. Distillation (Kugelrohr) of the residue afforded 0.37 g (86%) of **6a**: bp 75–80 °C (1 mmHg); n^{23}_D 1.4456; IR (neat) 1720 (C=O), 1615 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H, $SiMe_3$), 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 1.36 (m, 4 H, CH_2), 2.34 (m, 2 H, CH_2C=C), 3.71 (s, 3 H, OCH_3), 6.15 (t, J = 7.2 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ -1.44, 13.82, 22.30, 31.15, 31.40, 50.88, 135.68, 151.87, 170.92. Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.29; H, 10.48. The isomeric purity of the ester by GC (30-m SE-54 silica capillary column, 150 °C) was 98%.

Methyl (*E*)-2-(Trimethylsilyl)-4-cyclohexyl-2-butenoate (6b). Following the procedure above for the preparation of **6a**, the *Z* ester **1b** (0.51 g, 2.0 mmol) was isomerized in the presence of LDA. Distillation (Kugelrohr) yielded 0.4 g (78%) of the ester **6b**: bp 67–68 °C (10^{-2} mmHg); n^{25}_D 1.4712; IR (neat) 1720 (C=O), 1615 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H, $SiMe_3$), 0.85–1.69 (m, 11 H, cyclohexyl), 2.23 (t, J = 7.2 Hz, CH_2C=C), 3.71 (s, 3 H, OCH_3), 6.17 (t, J = 7.2 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ -1.34, 26.27, 26.41, 33.10, 37.88, 39.30, 50.97, 136.45, 150.57, 171.09; high-resolution MS m/z 254.1703 (calcd for $C_{14}H_{26}O_2Si$ 254.1702). The isomeric purity of the ester by GC (30-m DB-1701 silica capillary column, 130 °C) was 98%.

1-((Trimethylsilyl)oxy)-1-methoxy-2-(trimethylsilyl)-1,3-heptadiene (5a). Methyl (*E*)-2-(trimethylsilyl)-2-heptenoate (**6a**, 0.64 g, 3 mmol) was added to a freshly prepared solution of LDA (3.3 mmol) in THF at -78 °C. The light yellowish mixture formed was stirred for 2 h, treated with freshly distilled chlorotrimethylsilane (0.39 g, 3.6 mmol), and stirred at -78 °C for 0.5 h. The THF was removed under reduced pressure (10 mmHg) at room temperature, and the residue obtained was triturated with *n*-heptane (2 × 20 mL). While excluding air and moisture, the supernatant was transferred via a double-ended needle into an oven-dried sintered-glass funnel mounted on a round-bottom flask. The LiCl in the sintered glass funnel was rinsed with *n*-heptane (20 mL). The filtrate was concentrated and distilled (Kugelrohr) to furnished 0.75 g (87%) of **5a**: bp 50 °C (10^{-2} mmHg); n^{25}_D 1.4591; IR (neat) 1590 (C=C), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H, $SiMe_3$), 0.24 (s, 9 H, $OSiMe_3$), 0.89 (t, J = 7.2 Hz, 3 H, CH_3), 1.4 (m, 2 H, CH_2CH_3), 2.0 (m, 2 H, CH_2C=C), 3.48 (s, 3 H, OCH_3), 5.38 (dt, J = 15.9, 6.9 Hz, 1 H, CH=CCSi), 5.94 (dt, J = 15.9, 1.2 Hz, 1 H, C=CHCSi); ^{13}C NMR ($CDCl_3$) δ 0.16, 0.78, 13.79, 23.06, 36.02, 55.31, 92.54, 128.23, 128.75, 158.10; high-resolution MS m/z 286.1799 (calcd for $C_{14}H_{30}O_2Si_2$ 286.1784). GC analysis (30-m DB-5 silica capillary column, 160 °C) of the distillate revealed the presence of a single compound.

1-((Trimethylsilyl)oxy)-1-methoxy-2-(trimethylsilyl)-4-cyclohexyl-1,3-butadiene (5b). Following the procedure for the

preparation of **5a**, the *E* ester **6b** (0.25 g, 1.0 mmol) was converted to **5b** in 83% yield: bp 91–93 °C (10^{-2} mmHg); n^{24}_D 1.4787; IR (neat) 1580 (C=C), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (s, 9 H, $SiMe_3$), 0.24 (s, 9 H, $OSiMe_3$), 1.06–2.00 (m, 11 H, cyclohexyl), 3.48 (s, 3 H, OCH_3), 5.34 (dd, J = 16.5, 7.2 Hz, 1 H, CH=CCSi), 5.92 (dd, J = 16.5, 1.2 Hz, 1 H, C=CHCSi); ^{13}C NMR ($CDCl_3$) δ 0.17, 0.75, 26.12, 26.28, 33.40, 41.93, 55.25, 92.57, 125.32, 135.07, 157.99; high-resolution MS m/z 326.2097 (calcd for $C_{17}H_{34}O_2Si_2$ 326.2097).

1-((Trimethylsilyl)oxy)-1-methoxy-2-(trimethylsilyl)-3-(*N*,*N*-diisopropylamino)-1-heptene (7a). Freshly distilled diisopropylamine (0.13 g, 1.3 mmol) in THF (2 mL) was cooled to −78 °C, treated with 1.6 M solution of *n*-BuLi (0.76 mL, 1.2 mmol) in *n*-hexane, stirred at −78 °C for 15 min, warmed to 0 °C, and stirred for an additional 15 min. The reaction mixture was then cooled to −78 °C, treated with **1a** (0.21 g, 1.0 mmol), and stirred at −78 °C for 2 h. Trimethylsilyl chloride (0.20 mL, 1.5 mmol) was then added at −78 °C. The solution was gradually warmed to room temperature (23 °C) and stirred for 1 h. The solvents were removed under vacuum (~10 mmHg), and the residue obtained was diluted with *n*-heptane (10 mL). Under a blanket of N_2, the *n*-heptane solution was transferred via a double-ended needle into a sintered-glass funnel connected to a round-bottomed flask. The LiCl in the funnel was rinsed with *n*-heptane (2 × 5 mL), and the filtrate was concentrated and distilled (Kugelrohr) to furnish 0.33 g (94%) of **7a**: bp 100–102 °C (10^{-2} mmHg); n^{25}_D 1.4594; IR (neat) 1605 (C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 9 H, $SiMe_3$), 0.27 (s, 9 H, $OSiMe_3$), 0.90 (t, J = 7.2 Hz, 3 H, CH_3), 0.96 (d, J = 6.9 Hz, 6 H, $NCCH_3$), 1.03 (d, J = 6.3 Hz, 6 H, $NCCH_3$), 1.09–1.75 (m, 6 H, CH_2), 3.22 (m, 2 H, NCHMe), 3.48 (s, 3 H, OCH_3), 3.58 (m, 1 H, CHCSi); high-resolution (FAB) MS $(M + H)^+$ 388.3046 (calcd for $C_{20}H_{46}O_2Si_2N$ 388.3067).

Methyl (*E*)-2-(Trimethylsilyl)-2-methyl-3-heptenoate (11-1). To a freshly prepared solution of LDA (4.4 mmol) in THF (9 mL) at −78 °C was added **6a** (0.86 g, 4.0 mmol). The mixture was stirred at −78 °C for 2 h, treated with methyl iodide (1.7 g, 12 mmol, passed through neutral alumina and distilled over CaH_2 prior to use), stirred at −78 °C for 30 min and at 0 °C for 1 h, and then was poured into a separatory funnel containing a mixture of pentane (40 mL), a saturated solution of NH_4Cl (40 mL), and crushed ice (~40 g). The organic layer was separated, and the aqueous phase was extracted with pentane (40 mL). The combined pentane extracts were washed with 5% HCl (2 × 20 mL) and brine (2 × 40 mL) and dried over $MgSO_4$. Concentration and distillation (Kugelrohr) afforded 0.81 g (89%) of **11-1**: bp 88–89 °C (1 mmHg); n^{23}_D 1.4550; IR (neat) 1720 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.01 (s, 9 H, $SiMe_3$), 0.89 (t, J = 7.5 Hz, 3 H, CH_3), 1.30 (s, 3 H, CH_3CSi), 1.36 (m, 2 H, CH_2Me), 2.04 (m, 2 H, CH_2C=C), 3.66 (s, 3 H, OCH_3), 5.23 (dt, J = 15.9, 6.9 Hz, 1 H, CH=CCSi), 5.98 (dt, J = 15.9, 1.5 Hz, 1 H, C=CHCSi); ^{13}C NMR ($CDCl_3$) δ −4.09, 13.43, 15.09, 22.89, 34.99, 41.74, 51.02, 126.43, 130.24, 175.37. No ^{13}C NMR signals assignable to the *Z* isomer were detected. High-resolution MS m/z 228.1546 (calcd for $C_{12}H_{24}O_2Si$ 228.1547). The purity of the compound by GC (30-m SE-54 silica capillary column, 150 °C) was 99%.

Methyl (*E*)-2-(Trimethylsilyl)-2-butyl-3-heptenoate (11-2). Following the procedure for the preparation of **11-1**, the *E* ester **6a** (0.43 g, 2.0 mmol) was added at −78 °C to a freshly prepared solution of LDA (2.2 equiv) in THF. The resulting light yellowish mixture was stirred at −78 °C for 2 h, treated with *n*-butyl iodide (0.55 g, 3.0 mmol), and stirred for an additional 15 min at −78 °C and 2 h at 0 °C. Workup and distillation (Kugelrohr) yielded 0.46 g (85%) of **11-2**; bp 102–105 °C (1 mmHg); n^{25}_D 1.4572; IR (neat) 1700 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H, $SiMe_3$), 0.88 (m, 6 H, CH_3), 1.23–2.08 (m, 10 H, CH_2), 3.67 (s, 3 H, OCH_3), 5.20 (dt, J = 16.2, 6.9 Hz, 1 H, $CH{=}CCCO_2$), 5.85 (d, J = 16.2 Hz, $C{=}C^{-}[CCO_2]$); ^{13}C NMR ($CDCl_3$) δ −3.78, 13.54, 13.84, 23.00, 23.16, 27.09, 28.94, 35.32, 47.11, 50.88, 127.55, 127.57, 174.85; high-resolution MS m/z 270.2015 (calcd for $C_{15}H_{30}O_2Si$ 270.2015). The purity of the ester by GC (30-m SE-54 silica capillary column, 150 °C) was 96%.

Methyl (*E*)-2-(Trimethylsilyl)-2-methyl-4-cyclohexyl-3-butenoate (11-3). Following the procedure for the preparation of **11-1**, the *E* ester **6b** (0.25 g, 1.0 mmol) was added at −78 °C to a freshly prepared solution of LDA (1.1 equiv) in THF. The resulting light yellowish mixture was stirred at −78 °C for 2 h, treated with methyl iodide (0.43 g, 3.0 mmol), and stirred for an additional 30 min at −78 °C and 1 h at 0 °C. Workup and distillation (Kugelrohr) yielded 0.22 g (82%) of **11-3**: bp 60–63 °C (10^{-2} mmHg); n^{24}_D 1.4782; IR (neat) 1700 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.00 (s, 9 H, $SiMe_3$), 0.98–2.10 (m, 11 H, cyclohexyl), 1.23 (s, 3 H, CH_3), 3.67 (s, 3 H, OCH_3), 5.17 (dd, J = 16.2, 7.2 Hz, 1 H, $CH{=}CCCO_2$), 5.95 (dd, J = 16.2, 0.9 Hz, $C{=}CHCCO_2$); ^{13}C NMR ($CDCl_3$) δ −3.97, 15.09, 26.02, 26.11, 33.39, 33.58, 41.21, 51.26, 127.60, 132.75, 175.78; high-resolution MS m/z 268.1859 (calcd for $C_{15}H_{28}O_2Si$ 268.1859). The purity of the ester by GC (30-m DB-1701 silica capillary column, 150 °C) was 98%.

Methyl (*E*)-2-(Trimethylsilyl)-2-butyl-4-cyclohexyl-3-butenoate (11-4). Following the procedure for the preparation of **11-2**, the *E* ester **6b** (0.25 g, 1.0 mmol) was added at −78 °C to a freshly prepared solution of LDA (1.1 equiv) in THF. The resulting light yellowish mixture was stirred at −78 °C for 2 h, treated with *n*-butyl iodide (0.28 g, 1.5 mmol), and stirred for an additional 15 min at −78 °C and 2 h at 0 °C. Workup and distillation (Kugelrohr) yielded 0.22 g (71%) of **11-4**: bp 78–80 °C (10^{-2} mmHg); n^{23}_D 1.4774; IR (neat) 1700 (C=O), 970 (*trans*-C=C), 840 (C—Si) cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.03 (s, 9 H, $SiMe_3$), 0.85 (t, J = 7.2 Hz, 3 H, CH_3), 0.98–2.10 (m, 17 H, cyclohexyl and CH_2), 3.64 (s, 3 H, OCH_3), 5.14 (dd, J = 16.2, 7.2 Hz, 1 H, $CH{=}CCCO_2$), 5.81 (d, J = 16.2 Hz, $C{=}CHCCO_2$); ^{13}C NMR ($CDCl_3$) δ −3.68, 13.91, 23.20, 26.07, 26.20, 27.07, 28.87, 33.46, 33.51, 41.50, 47.00, 50.98, 124.92, 133.82, 175.06; high-resolution MS m/z 310.2336 (calcd for $C_{18}H_{34}O_2Si$ 310.2328). The purity of the ester by GC (30-m DB-1701 silica capillary column, 150 °C) was 98%.

Methyl (*E*)-2-Methyl-3-heptenoate (13-1). To dry methanol (1 mL, 25 mmol) in THF (2 mL) was added at 0 °C a 1.6 M solution (0.70 mL, 1.1 mmol) of *n*-BuLi in *n*-hexane. The resultant LiOMe was stirred for 15 min, treated with **11-1** (0.23 g, 1.0 mmol), and stirred for 30 min at 0 °C. The mixture was then poured into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The organic layer was separated, and the aqueous phase was extracted with pentane. The combined pentane extracts were washed with 5% HCl (2 × 10 mL) and brine (2 × 20 mL) and dried over $MgSO_4$. Concentration and distillation (Kugelrohr) afforded 0.13 g (83%) of **13-1**: bp 70–73 °C (2 mmHg); n^{25}_D 1.4282; IR (neat) 1740 (C=O), 970 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, J = 7.5 Hz, 3 H, CH_3), 1.23 (d, J = 6.9, 3 H, CH_3CCO_2), 1.36–1.99 (m, 4 H, CH_2), 3.10 (m, 1 H, $CHCO_2$), 3.67 (s, 3 H, OCH_3), 5.50 (m, 2 H, CH=CH); ^{13}C NMR ($CDCl_3$) δ 13.54, 17.47, 22.27, 34.43, 42.77, 51.72, 128.86, 132.07, 175.54. No ^{13}C NMR signals assignable to the stereoisomer were detected. High-resolution MS m/z 156.1145 (calcd for $C_9H_{16}O_2$ 156.1150). The purity of the ester by GC (30-m SE-54 silica capillary column, 110 °C) was 99%.

Methyl (*E*)-2-Butyl-3-heptenoate (13-2). Following the above procedure for the preparation of **13-1**, the *E* ester **11-2** (0.27 g, 1.0 mmol) was added at −78 °C to a freshly prepared solution of LiOMe in THF. The resulting mixture was stirred at 0 °C for 30 min. Workup and distillation (Kugelrohr) yielded 0.16 g (81%) of **13-2**: bp 62–64 °C (2 mmHg); n^{23}_D 1.4377; IR (neat) 1740 (C=O), 970 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, J = 7.2 Hz, 6 H, CH_3), 1.10–1.80 (m, 8 H, CH_2), 1.98 (m, 2 H, CH_2C=C), 2.93 (m, 1 H, $CHCO_2$), 3.66 (s, 3 H, OCH_3), 5.38 (dd, J = 15.3, 8.4 Hz, 1 H, $C{=}CHCCO_2$), 5.51 (dt, J = 15.3, 6.6 Hz, 1 H, $CH{=}CCCO_2$); ^{13}C NMR ($CDCl_3$) δ 13.17, 13.50, 22.39, 29.41, 32.48, 34.49, 49.21, 51.03, 128.52, 132.85, 174.73; high-resolution MS m/z 198.1608 (calcd for $C_{12}H_{22}O_2$ 198.1620). The purity of the ester by GC (30-m SE-54 silica capillary column, 150 °C) was 96%.

Methyl (*E*)-2-Butyl-4-cyclohexyl-3-butenoate (13-4). Following the above procedure for the preparation of **13-1**, the *E* ester **11-4** (0.31 g, 1.0 mmol) was added at −78 °C to a freshly prepared solution of LiOMe in THF. The resulting mixture was stirred at 0 °C for 30 min. Workup and distillation (Kugelrohr) yielded 0.19 g (80%) of **13-4**: bp 89–91 °C (2 mmHg); n^{23}_D 1.4637; IR (neat) 1740 (C=O), 970 (*trans*-C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, J = 6.9 Hz, 3 H, CH_3), 0.89–1.80 (m, 16 H, cyclohexyl

and CH_2), 1.92 (m, 1 H, CHC=CCCO$_2$), 2.90 (m, 1 H, CHCO$_2$), 3.66 (s, 3 H, OCH_3), 5.35 (dd, J = 15.6, 8.4, Hz, 1 H, C=CHCCO$_2$), 5.46 (dd, J = 15.6, 6.3, Hz, 1 H, CH=CCCO$_2$); ^{13}C NMR ($CDCl_3$) δ 13.86, 22.35, 25.95, 26.12, 29.21, 32.41, 32.81, 32.86, 40.50, 49.21, 51.50, 125.21, 139.08, 175.26; high-resolution MS m/z 238.1915 (calcd for $C_{15}H_{26}O_2$ 238.1933). The purity of the ester by GC (30-m DB-1701 silica capillary column, 150 °C) was 99%.

Methyl (*E*)-2-Methyl-2-heptenoate (14-1). Into a dry, two-neck flask equipped with a magnetic stirrer and a thermometer were placed 11-1 (0.23 g, 1.0 mmol) and dry THF (2.0 mL). To this was added dropwise at 0 °C a 1 M solution of n-Bu_4NF (1.1 mL, Aldrich) in THF. The mixture was stirred at 0 °C for 1 h, treated with H_2O (1.0 mL), stirred for 15 min, and then was poured into a separatory funnel containing a mixture of pentane (20 mL), a saturated solution of NH_4Cl (20 mL), and crushed ice (~20 g). The phases were separated, and the organic phase was washed with 5% HCl (2 × 10 mL) and brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. Distillation (Kugelrohr) afforded 0.12 g (75%) of 14-1: bp 65–70 °C (2 mmHg); $n^{25}$$_D$ 1.4433; IR (neat) 1720 (C=O), 1650 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.9 Hz, 3 H, CH_3), 1.40 (m, 4 H, CH_2), 1.82 (s, 3 H, C=CCH_3), 2.18 (m, 2 H, CH_2C=C), 3.73 (s, 3 H, OCH_3), 6.77 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 12.28, 13.82, 22.37, 28.31, 30.65, 51.57, 127.34, 142.71, 168.68; high-resolution MS m/z 156.1150 (calcd for $C_9H_{16}O_2$ 156.1150). No ^{13}C NMR signals assignable to the Z isomer could be detected. The purity of the ester by GC (30-m SE-54 silica capillary column, 150 °C) was 97%.

Methyl (*E*)-2-Butyl-2-heptenoate (14-2). Following the above procedure for the preparation of 14-1, a 1 M solution of n-Bu_4NF (1.6 mL, Aldrich) in THF was added to the E ester 11-2 (0.41 g, 1.5 mmol) in THF (3.0 mL). The mixture was stirred at 0 °C for 1 h, treated with H_2O (1.5 mL), and stirred for 15 min. Workup and distillation (Kugelrohr) yielded 0.2 g (74%) of a 96:4 mixture of 14-2 and 13-2: bp 72–74 °C (2 mmHg); $n^{24}$$_D$ 1.4482; IR (neat) 1710 (C=O), 1640 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (m, 6 H, CH_3), 1.33 (m, 8 H, CH_2), 2.15 (m, 2 H, C=CCH_2), 2.30 (m, 2 H, C=CCH_2), 3.72 (s, 3 H, OCH_3), 6.75 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 13.83, 13.88, 22.43, 22.64, 26.50, 28.19, 31.00, 31.54, 51.45, 132.37, 142.65, 168.53; high-resolution MS m/z 198.1616 (calcd for $C_{12}H_{22}O_2$ 198.1620). The purity of the ester by GC (30-m SE-54 silica capillary column, 160 °C) was 94%.

Methyl (*E*)-2-Butyl-4-cyclohexyl-2-butenoate (14-4). Following the above procedure for the preparation of 14-1, a 1 M solution of n-Bu_4NF (1.1 mL, Aldrich) in THF was added to the E ester 11-4 (0.31 g, 1.0 mmol) in THF (2.0 mL). The mixture was stirred at 0 °C for 1 h, treated with H_2O (1.0 mL), and stirred for 15 min. Workup and distillation (Kugelrohr) yielded 0.20 g (84%) of a 98:2 mixture of 14-4 and 13-4: bp 105–110 °C (0.5 mmHg); $n^{23}$$_D$ 1.4760; IR (neat) 1710 (C=O), 1640 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.80 (m, 18 H, cyclohexyl and C_3H_7), 2.05 (t, J = 7.5 Hz, 2 H, CH_2CCO), 2.27 (m, 2 H, CH_2C=C), 3.71 (s, 3 H, OCH_3), 6.75 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 13.87, 22.63, 26.20, 26.30, 26.49, 31.43, 33.24, 36.20, 37.83, 51.42, 132.74, 141.49, 168.41; high-resolution MS m/z 238.1932 (calcd for $C_{15}H_{26}O_2$ 238.1933). The purity of the ester by GC (30-m DB-210 silica capillary column, 170 °C) was 97%.

Methyl (*E*)-3-*n*-Butyl-4-(methoxycarbonyl)-4-nonenoate (20). To a solution of 3a (0.87 g, 4.1 mmol) in THF (8 mL) cooled in an ice–water bath was added a 1.0 M solution of n-Bu_4NF in THF (4.5 mL). The mixture was stirred at ~4 °C for 1 h, treated with H_2O (4 mL), stirred for 15 min at ~4 °C, and then poured into a separatory funnel containing a mixture of pentane, a saturated solution of NH_4Cl, and crushed ice (~20 g). The phases were separated, the aqueous phase was extracted with pentane (80 mL), and the combined organic phases were washed with 5% HCl (2 × 20 mL) and brine (2 × 20 mL), dried ($MgSO_4$), and concentrated. Purification of the residue (90% yield) by flash column chromatography[27] on silica gel using methylene chloride as eluant afforded the diester 20 (58%): bp 76–78 °C (5 × 10^{-3} mmHg); $n^{26}$$_D$ 1.4550; IR (neat) 1730, 1700 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 7.2 Hz, 3 H, CH_3), 0.90 (t, J = 6.9 Hz, 3 H, CH_3), 1.05–1.80 (m, 10 H, CH_2), 2.22 (m, 2 H, CH_2C=C), 2.56 (dd, J = 15, 6.6 Hz, 1 H, CHCO$_2$), 2.69 (dd, J = 15, 8.4 Hz, 1 H, CHCO$_2$), 3.10 (m, 1 H, CHCCO$_2$), 3.60 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 6.78 (t, J = 7.5 Hz, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 13.73, 13.81, 22.39, 22.52, 28.06, 29.94, 30.98, 32.93, 34.96, 38.63, 51.08, 51.14, 132.86, 144.92, 167.35, 173.25; high-resolution (FAB) GC–MS (M + H)$^+$ of the main peak 285.2068 (calcd for $C_{16}H_{29}O_4$ 285.2067). GC analysis (30-m DB-210 silica capillary column, 180 °C) of the distillate revealed that the compound was ~90% pure.

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Supplementary Material Available: High-field ^{1}H NMR spectra for 1b, 1c, 3b, 3c, 4c, 6b, 5a, 5b, 7a, 11-1, 11-2, 11-3, 11-4, 13-1, 13-2, 13-4, 14-1, 14-2, 14-4, and 20 (20 pages). Ordering information is given on any current masthead page.

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Enantioselective Total Synthesis of the Mycotoxin (-)-Talaromycin B by a Hetero Diels–Alder Reaction[1]

Lutz F. Tietze* and Christoph Schneider

Institut für Organische Chemie, Georg-August-Universität, D-3400 Göttingen, Federal Republic of Germany

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(-)-Talaromycin B was formed in an overall yield of 5% in nine steps via a hetero Diels–Alder reaction of the exocyclic vinyl ether 3 and methyl *O*-benzoyldiformylacetate (4) as the key transformation. The enantiomerically pure vinyl ether 3 was prepared in 28% yield and ee >98% by alkylation of the *N*-butyryloxazolidinone 5 with 1-bromo-4-(trimethylsilyl)-2-butyne (6), followed by a reduction–hydrogenation–protodesilylation sequence to give 9, which was transformed into 3 by iodoetherification with iodine and elimination with DBU. Methyl *O*-benzoyldiformylacetate (4) was synthesized by formylation of methyl 3,3-dimethoxypropionate, followed by benzoylation. The cycloaddition of 3 and 4 gave predominantly the desired adduct 11 together with the other three possible diastereomers. (-)-Talaromycin B (2) was obtained from 11 by reduction with DIBAL-H and stereoselective hydrogenation with platinum as catalyst. For purification purposes, 2 was transformed into a cyclic silyl ether by reaction with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane.

The highly toxic mycotoxins talaromycin A (1) and B (2) were discovered by Lynn[2] in 1982 as the first spiroacetals of fungal origin. This unique structural feature occurs in many natural products, e.g., polyether antibiotics,

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