Copper Chloride-Catalyzed and Hydrochloric Acid-Mediated Chemoselective Protiodestannylations of Alkyl (*Z*)- or (*E*)-2,3-Bis(trimethylstannyl)-2-alkenoates. Stereoselective Preparation of Alkyl (*E*)- and (*Z*)-3-Trimethylstannyl-2-alkenoates

Edward Piers,* Ernest J. McEachern, and Miguel A. Romero

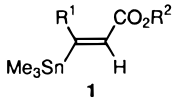
Department of Chemistry, University of British Columbia, 2036 Main Mall, University Campus, Vancouver, British Columbia, Canada V6T 1Z1

Received April 30, 1997[⊗]

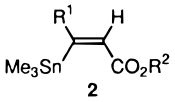
Treatment of alkyl (*Z*)-2,3-bis(trimethylstannyl)-2-alkenoates (**7**) with a catalytic amount of copper(I) chloride in *N*,*N*-dimethylformamide (DMF) containing a small quantity of water provides very good-to-excellent yields of alkyl (*E*)-3-trimethylstannyl-2-alkenoates (**1**). On the other hand, stirring of solutions of alkyl (*Z*)- (**7**) or (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates (**8**) in DMF containing dilute hydrochloric acid produces, efficiently, alkyl (*Z*)-3-trimethylstannyl-2-alkenoates (**2**).

Introduction

The synthetic uses of alkyl (*E*)- and (*Z*)-3-trialkylstannnyl-2-alkenoates of general structures **1** and **2**, along with those of substances readily derived from **1** and **2**, are well established.[1,2] Up to the present time, the



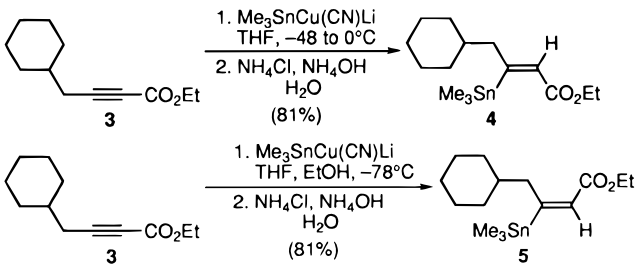
1



2

most convenient and efficient methods for preparing **1** and **2** in a stereocontrolled fashion entail treatment of α,β-alkynic esters with suitable trialkylstannylcopper(I) reagents under carefully defined reaction conditions.[1a,3] Examples involving the production of diastereomeric 3-trimethylstannyl-2-alkenoates are shown in Scheme 1.[3e] Thus, reaction of ethyl 4-cyclohexyl-2-butynoate (**3**) with lithium (trimethylstannyl)(cyano)cuprate[4] in tetrahydrofuran (THF) at −48 to 0 °C, followed by addition of aqueous NH_4Cl-NH_4OH (pH ∼8), provided the (*Z*)-3-trimethylstannyl-2-alkenoate **4**, accompanied by small amounts (∼5% total) of the corresponding *E* isomer and ethyl (*E*)-4-cyclohexyl-2,3-bis(trimethylstannyl)-2-butenoate. Purification of this material by a combination of flash chromatography[5] and distillation afforded **4** in 81% yield.[3e] On the other hand, treatment (THF, −78 °C) of **3** with the same cuprate reagent *in the presence of dry ethanol*, followed by a suitable workup and chromatographic separation of the small amount (<5%) of **4** from the major product **5**, provided the latter material (81%).[3e] Other trimethylstannylcopper(I) reagents can also be employed to effect conversions analogous to those summarized in Scheme 1.[3a−d]

Scheme 1



Reports[6] from this laboratory have described, *inter alia*, the efficient palladium(0)-catalyzed addition of hexamethyldistannane to α,β-alkynic esters **6**. The products of these processes, alkyl (*Z*)-2,3-bis(trimethylstannyl)-2-alkenoates **7**, are produced in good-to-excellent yields (Scheme 2). It has also been disclosed[6] that compounds **7** are thermally unstable and, upon heating at 75−90 °C, rearrange cleanly to the corresponding *E* isomers **8**. We report herein that treatment of compounds **7** with a catalytic amount of copper(I) chloride in wet *N*,*N*-dimethylformamide (DMF) at room temperature effects the chemo- and stereoselective removal of the 2-trimethyl-

* Telephone: 604-822-3219. Fax: 604-822-2847. E-mail: epier@unixg.ubc.ca.

[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1997.

(1) (a) Piers, E.; Chong, J. M.; Gustafson, K.; Andersen, R. J. *Can. J. Chem.* **1984**, *62*, 1. (b) Piers, E.; Gavai, A. V. *J. Chem. Soc., Chem. Commun.* **1985**, 1241. (c) Piers, E.; Gavai, A. V. *Tetrahedron Lett.* **1986**, *27*, 313. (d) Piers, E.; Friesen, R. W. *J. Org. Chem.* **1986**, *51*, 3405. (e) Piers, E.; Friesen, R. W. *Can. J. Chem.* **1987**, *65*, 1681. (f) Piers, E.; Lu, Y.-F. *J. Org. Chem.* **1988**, *53*, 926. (g) Piers, E.; Llinas-Brunet, M. *J. Org. Chem.* **1989**, *54*, 1483. (h) Piers, E.; Gavai, A. V. *J. Org. Chem.* **1990**, *55*, 2374. (i) Piers, E.; Gavai, A. V. *J. Org. Chem.* **1990**, *55*, 2380. (j) Piers, E.; Friesen, R. W. *Can. J. Chem.* **1992**, *70*, 1204. (k) Piers, E.; Friesen, R. W.; Rettig, S. J. *Can. J. Chem.* **1992**, *70*, 1385. (l) Piers, E.; Roberge, J. Y. *Tetrahedron Lett.* **1992**, *33*, 6923. (m) Piers, E.; Ellis, K. A. *Tetrahedron Lett.* **1993**, *34*, 1875. (n) Piers, E.; Wong, T. *J. Org. Chem.* **1993**, *58*, 3609. (o) Piers, E.; Llinas-Brunet, M.; Oballa, R. M. *Can. J. Chem.* **1993**, *71*, 1484. (p) Piers, E.; Wai, J. S. M. *Can. J. Chem.* **1994**, *72*, 146. (q) Piers, E.; Coish, P. D. *Synthesis* **1995**, 47. (r) Piers, E.; McEachern, E. J.; Burns, P. A. *J. Org. Chem.* **1995**, *60*, 2322. (s) Piers, E.; McEachern, E. J.; Romero, M. A. *Tetrahedron Lett.* **1996**, *37*, 1173. (t) Piers, E.; Romero, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 1215. (u) Piers, E.; McEachern, E. J. *Synlett* **1996**, 1087.

(2) (a) Harusawa, S.; Osaki, H.; Takemura, S.; Yoneda, R.; Kurihara, T. *Tetrahedron Lett.* **1992**, *33*, 2543. (b) Dodd, D. S.; Pierce, H. D. Jr.; Oehlschlager, A. C. *J. Org. Chem.* **1992**, *57*, 5250. (c) Paquette, L. A.; Lassalle, G. Y.; Lovely, C. J. *J. Org. Chem.* **1993**, *58*, 4254. (d) Paquette, L. A.; Deaton, D. N.; Endo, Y.; Poupart, M.-A. *J. Org. Chem.* **1993**, *58*, 4262. (e) Harusawa, S.; Takemura, S.; Osaki, H.; Yoneda, R.; Kurihara, T. *Tetrahedron* **1992**, *49*, 7657. (f) De Brabander, J.; Vandewalle, M. *Synthesis* **1994**, 855. (g) Elbaum, D.; Porco, J. A. Jr.; Stout, T. J.; Clardy, J.; Schreiber, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 211. (h) Reginato, G.; Capperucci, A.; Degl'Innocenti, A.; Pecchi, S. *Tetrahedron* **1995**, *51*, 2129. (i) Hutzinger, M. W.; Oehlschlager, A. C. *J. Org. Chem.* **1995**, *60*, 4595.

(3) (a) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263. (b) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, *22*, 4905. (c) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron* **1989**, *45*, 363. (d) Piers, E.; Tillyer, R. D. *J. Org. Chem.* **1988**, *53*, 5366. (e) Piers, E.; Wong, T.; Ellis, K. A. *Can. J. Chem.* **1992**, *70*, 2058.

(4) Piers, E.; Morton, H. E.; Chong, J. M. *Can. J. Chem.* **1987**, *65*, 78.

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

(6) (a) Piers, E.; Skerlj, R. T. *J. Chem. Soc., Chem. Commun.* **1986**, 626. (b) Piers, E.; Skerlj, R. T. *Can. J. Chem.* **1994**, *72*, 2468.

S0022-3263(97)00769-X CCC: $14.00

Scheme 2

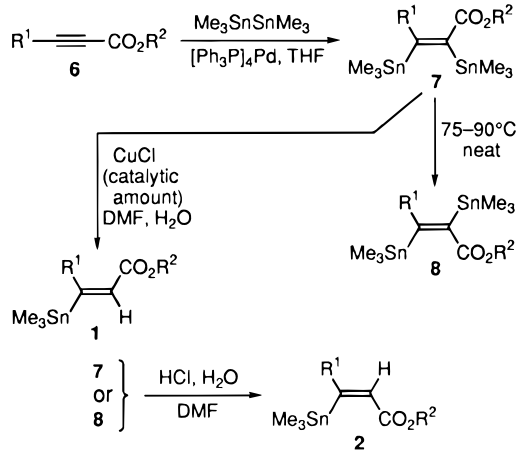
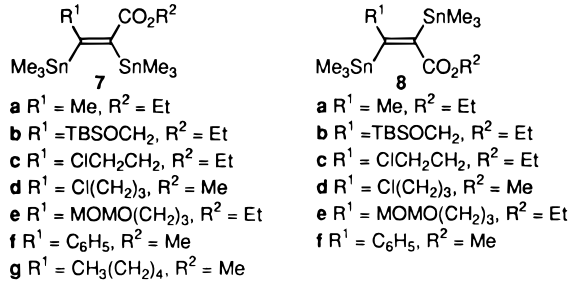
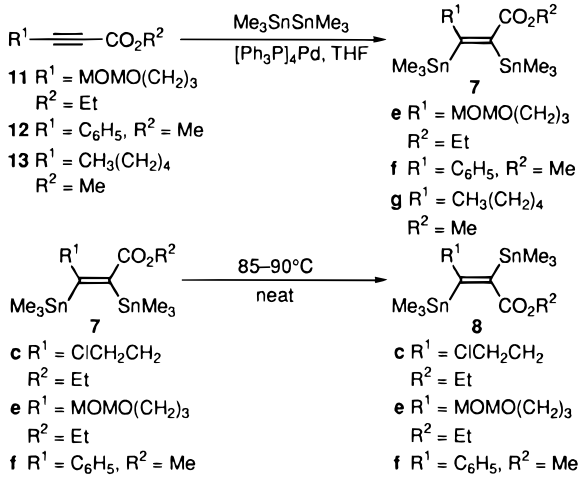


Chart 1



Scheme 3

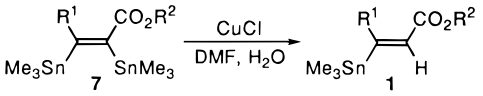


stannyl function to produce excellent yields of the corresponding alkyl (*E*)-3-trimethylstannyl-2-alkenoates **1**. On the other hand, reaction of **7** or **8** with 1.2 equiv of 1 N hydrochloric acid in DMF also results in the chemoselective removal of the α-Me_3Sn group, but in these cases the products are the *Z* alkenoates **2** (Scheme 2).

Results and Discussion

(a) The Substrates. The structural formulas of the alkyl (*Z*)- (**7a**−**g**) and (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates (**8a**−**f**) employed in this study are given in Chart 1. Of these substances, the *Z* isomers **7a**−**d** and the *E* isomers **8a**, **b**, and **d** have been reported previously.[6b] Compounds **7e**−**g** were prepared via Pd(0)-catalyzed addition of hexamethyldistannane to the α,β-alkynic esters **11**−**13**, respectively (Scheme 3).[6b] The substrates **12** and **13** are commercially available, while **11** was readily prepared in two steps from 4-pentyn-1-ol (see Experimental Section). Thermolysis of each of the substances **7c** (neat, 90 °C, 18 h), **7e** (neat, 90 °C, 24 h), and **7f** (neat, 85 °C, 26 h) resulted in the efficient production of the corresponding *E* alkenoates **8c**, **e**, and **f** (Scheme 3). Of the latter materials, **8c** and **8d** were used without purification, while **8f** was fully characterized.

Table 1. CuCl-Catalyzed Protiodestannylation of Alkyl (*Z*)-2,3-Bis(trimethylstannyl)-2-alkenoates[a]



entry	substrate (mmol)	R^1 [b]	CuCl, mmol	DMF, mL	H_2O, mL	product (yield, %)[c]
1	**7a** (0.45)	Me	0.005	4.0	0.40	**1a** (91)
2	**7b** (0.35)	$TBSOCH_2$	0.004	4.0	0.40	**1b** (94)
3	**7c** (0.44)	$ClCH_2CH_2$	0.004	4.0	0.40	**1c** (78)
4	**7d** (0.41)	$Cl(CH_2)_3$	0.004	4.0	0.40	**1d** (87)
5	**7e** (0.39)	$MOMO(CH_2)_3$	0.004	4.0	0.40	**1e** (90)
6[d]	**7f** (0.10)	C_6H_5	0.004	1.1	0.15	**1f** (75)
7	**7g** (1.49)	$CH_3(CH_2)_4$	0.016	15.0	2.60	**1g** (91)

[a] Unless otherwise noted, all reactions were carried out at room temperature for 2 h. [b] R^2 = Et for **7a**−**c** and **7e**; R^2 = Me for **7d**, **7f**, and **7g**. [c] Yield of purified **1**. In each case, **1** was accompanied by minor amounts (2−7%, based on GLC analysis) of the corresponding alkyl (*Z*)-3-trimethylstannyl-2-alkenoate. [d] In this case, the reaction time was 30 min.

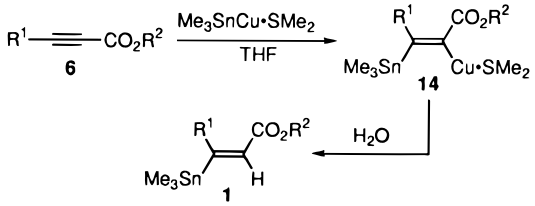
(b) CuCl-Catalyzed Protiodestannylation of the Alkyl (*Z*)-2,3-Bis(trimethylstannyl)-2-alkenoates (7a−g). Treatment (room temperature, 2 h) of the bis(trimethylstannane) **7a** with approximately 1 mol % of CuCl in DMF containing water (~10% by volume) gave a mixture of ethyl (*E*)-3-trimethylstannyl-2-butenoate (**1a**) and the corresponding *Z* isomer in a ratio of ~98:2. Flash chromatography[5] of this mixture on silica gel provided **1a** in 91% yield (Table 1, entry 1). In a similar fashion, the substrates **7b**−**g** were transformed into the protiodestannylated products **1b**−**g** in very good-to-excellent yields (Table 1, entries 2−7). In each of the conversions, the major product was accompanied by a small amount of the *Z* isomer, but in no case was the latter material formed in an amount greater than ~7% of the product mixture (see footnote *c*, Table 1). It should also be mentioned that, in general, alkyl (*E*)- and (*Z*)-3-trimethylstannyl-2-alkenoates are readily separated by chromatography on silica gel and, therefore, the acquisition of either isomer in pure form is easily achieved.

Of the products **1a**−**g** given in Table 1, three (**1a**,[3c] **1b**,[3c] **1d**[3e]) have been reported previously. Full characterization data for the remaining substances are presented in the Experimental Section.

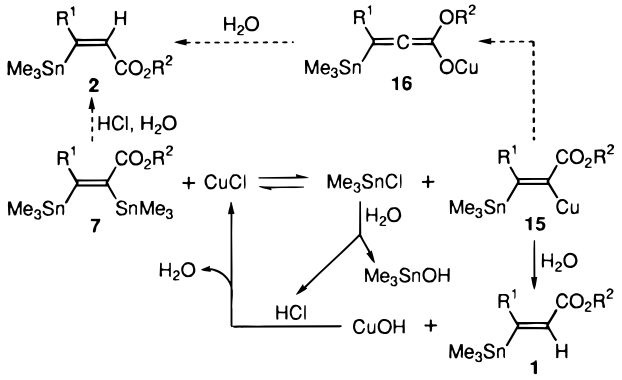
On the basis of previous studies,[7] it is clear that, in alkyl (*Z*)-2,3-bis(trimethylstannyl)-2-alkenoates (**7**), the alkenyl−tin bond associated with the α-trimethylstannyl group is much more labile than that related to the β-Me_3Sn function. It has also been established[8] that a trialkylstannyl group attached to a carbon−carbon double bond readily undergoes (reversible) transmetalation with copper(I) salts to produce the corresponding alkenylcopper(I) intermediate. Finally, there is strong evidence for the conclusion that intermediates of general structure **14**, derived from the cis addition of $Me_3SnCu{\cdot}SMe_2$ to α,β-

(7) Piers, E.; Skerlj, R. T. *J. Org. Chem.* **1987**, *52*, 4421.
(8) Farina, V.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905.

Scheme 4



Scheme 5

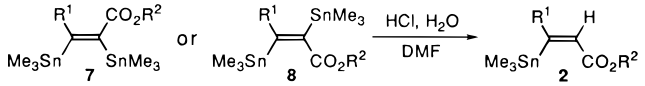


alkynic esters **6**, are configurationally quite stable and undergo protonation of the alkenyl−copper bond with retention to produce the *E* alkenoates **1** (Scheme 4).[3c] On the basis of these findings, it is reasonable to propose that the Cu(I)-catalyzed protiodestannylation of substances of general structure **7** proceeds via the pathway shown in Scheme 5. Thus, treatment of **7** with CuCl in DMF would be expected to result in transmetalation of the α-trimethylstannyl function to afford Me_3SnCl and the alkenylcopper(I) intermediate **15**, which would be protonated by water with retention of configuration to afford **1**. Reaction of the resultant CuOH with HCl (formed from $Me_3SnCl + H_2O \rightarrow Me_3SnOH + HCl$) would regenerate the CuCl catalyst. The small amount of the geometric isomer **2** formed from the overall protiodestannylation process (Table 1) is, perhaps, due to a (minor) pathway involving isomerization of **15** to the copper(I) allenoate **16**, which subsequently protonates on the central allenic carbon from the side opposite to the bulky Me_3Sn function. Alternatively, the minor amounts of **2** could be formed by HCl-catalyzed protiodestannylation of **7** (vide infra).

It should be noted that the CuCl−catalyzed protiodestannylations of alkyl (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates (**8**, Chart 1) are not synthetically useful reactions. In general, the conversions are not clean and the isolated yields of the expected products, alkyl (*Z*)-3-trimethylstannyl-2-alkenoates, are poor. Analyses of the crude reaction mixtures indicate that the two Me_3Sn functions are competitively removed. It thus appears that the alkenyl−tin bonds associated with the β-Me_3Sn group in the *E* isomers **8** are more labile than the corresponding carbon−tin bonds in the *Z* substrates **7**. This is, perhaps, due to the fact that intramolecular coordination of the ester carbonyl oxygen in **8** with the β-Sn atom (vide infra) weakens the alkenyl−tin bond.

(c) Hydrochloric Acid-Mediated Protiodestannylation of Alkyl (*Z*)- (7a−f) and (*E*)-2,3-Bis(trimethylstannyl)-2-alkenoates (8a−f). The results of these experiments are summarized in Table 2. When the substrate **7a** was treated with dilute hydrochloric acid in DMF at room temperature, a mixture of ethyl (*Z*)-3-trimethylstannyl-2-butenoate (**2a**) and the corresponding geometric isomer (**1a**, see footnote *c*, Table 2) was produced in high yield. The ratio of the two products was ∼4:1, respectively, and, after flash chromatography on silica gel, the major isomer was isolated in 80% yield (Table 2, entry 1). Similarly, protiodestannylation of the 2,3-bis(trimethylstannyl)-2-alkenoates **7b−f** gave the products **2b−f**, respectively, in yields ranging from 76% (**2e**, entry 5) to 94% (**2f**, entry 6). For the reactions summarized in Table 2, entries 1−6, the amounts of minor products (alkyl (*E*)-3-trimethylstannyl-2-alkenoates **1**) present in the product mixtures varied from ∼5% (entry 6) to ∼20% (entry 5).

Table 2. Hydrochloric Acid-Mediated Protiodestannylation of Alkyl (*Z*)- and (*E*)-2,3-Bis(trimethylstannyl)-2-alkenoates[a]



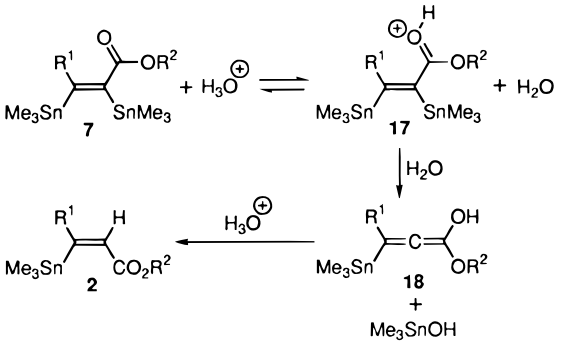
entry	substrate (mmol)	R^1 [b]	1 N HCl, mL	DMF, mL	reaction time, min	product (yield, %)[c]
1	**7a** (0.45)	Me	0.55	9.0	60	**2a** (80)
2	**7b** (0.35)	$TBSOCH_2$	0.35	8.0	5	**2b** (85)
3	**7c** (0.41)	$ClCH_2CH_2$	0.49	8.0	60	**2c** (83)
4	**7d** (0.41)	$Cl(CH_2)_3$	0.49	8.0	60	**2d** (81)
5	**7e** (0.39)	$MOMO(CH_2)_3$	0.46	8.0	30	**2e** (76)
6	**7f** (0.13)	C_6H_5	0.16	3.0	10	**2f** (94)
7	**8a** (0.45)	Me	0.55	9.0	180	**2a** (95)
8	**8b** (0.35)	$TBSOCH_2$	0.35	8.0	2	**2b** (74)
9	**8c** (0.53)	$ClCH_2CH_2$	0.64	10.0	60	**2c** (79)[d]
10	**8d** (0.20)	$Cl(CH_2)_3$	0.25	4.0	60	**2d** (91)
11	**8e** (0.39)	$MOMO(CH_2)_3$	0.46	8.0	60	**2e** (82)[d]
12	**8f** (0.33)	C_6H_5	0.38	6.4	180	**2f** (87)

[a] All reactions were carried out at room temperature. [b] R^2 = Et for **7a−c**, **7e**, **8a−c**, and **8e**; R^2 = Me for **7d**, **7f**, **8d**, and **8f**. [c] Yield of purified **2**. In each case, **2** was accompanied by minor amounts (entries 1−6, ∼5−20%; entries 7−12, <1−5%, based on GLC analyses) of the corresponding alkyl (*E*)-3-trimethylstannyl-2-alkenoate. [d] These numbers refer to combined yields for the thermal conversion of the (*Z*)-bis(trimethylstannyl)alkenoates **7c** and **7e**, respectively, to the corresponding *E* isomers, followed by acid-promoted protiodestannylation of the crude material thus obtained.

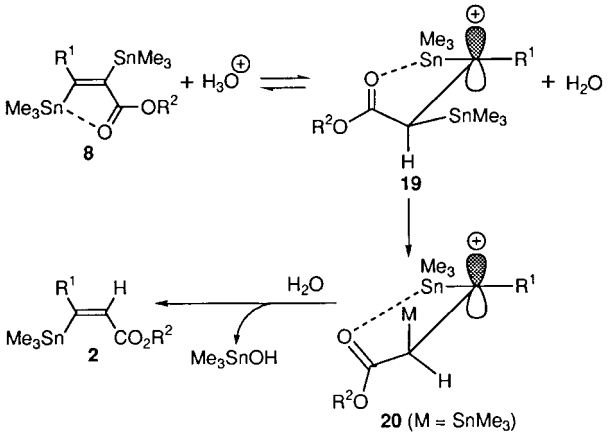
The hydrochloric acid-mediated protiodestannylation of the alkyl (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates (**8a−f**) also proceeded smoothly and afforded very good-to-excellent yields of the corresponding products **2a−f** (Table 2, entries 7−12). Again, the latter materials were accompanied by small amounts of the *E* isomers, ranging from <1% (entry 12) to ∼5% (entries 8 and 11). Interestingly, the quantities of these "side-products" obtained from treatment of **8** with dilute hydrochloric acid were generally lower than those derived from destannylation of **7** via an identical protocol (see Table 2, footnote *c*).

Of the products **2a−f** listed in Table 2, **2a**,[3c] **2b**,[3c] and **2d**[3e] were reported previously, while substances **2c**, **2e**, and **2f** were prepared for the first time during the course of this study. The preparation of **2c** is particularly noteworthy. Reactions of ethyl 5-chloro-2-pentynoate with lithium (trimethylstannyl)(phenylthio)cuprate[3c] or lithium (trimethylstannyl)(cyano)cuprate,[3e] under conditions that generally transform alkyl α,β-alkynic esters into alkyl (*Z*)-3-trimethylstannyl-2-alkenoates efficiently, produce **2c** in very poor yields. In contrast, as can be seen from Table 2, the yields of **2c** via the protiodestannylation routes are very good. It should also be noted that the acquisition of products **2b** and **2e** shows that

Scheme 6



Scheme 7



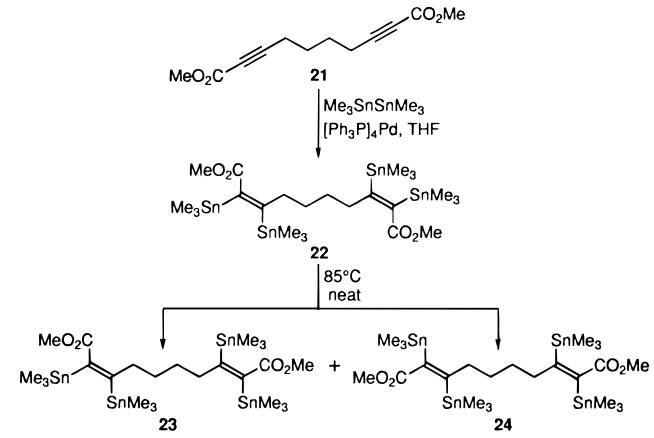
the new method can be employed successfully for the synthesis of compounds containing acid-labile functional groups.

The acid-mediated protiodestannylation of the *Z* alkenoates **7** (Table 2, entries 1−6) probably occurs via a pathway as outlined in Scheme 6.[9] Protonation of **7** on the oxygen of the ester carbonyl, followed by nucleophilic attack on the α-Me_3Sn function of the resultant intermediate **17**, would provide the allenol **18**. The stereoselective formation of the major product **2** would result from preferential protonation at C-2 of **18** from the side opposite to the sterically bulky Me_3Sn function.

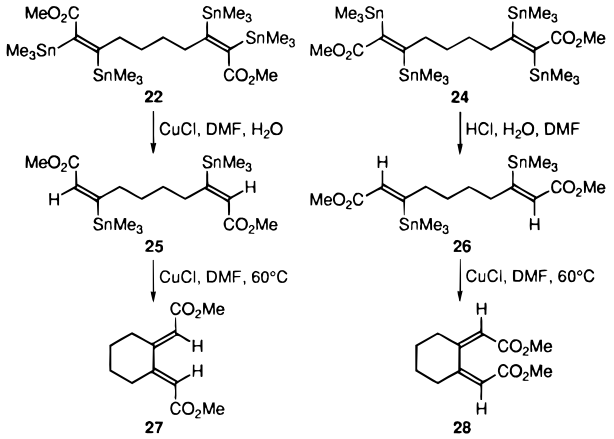
Protiodestannylation of the *E* alkenoates **8** may be mechanistically somewhat more complex. It is certainly possible that this process proceeds, at least partially, via a pathway analogous to that presented in Scheme 6. However, the fact that destannylation of **8** is consistently more stereoselective (in favor of the *Z* alkenoate **2**, see Table 2) than that observed for the geometrically isomeric substrates **7** suggests that an alternative pathway is, at least to some degree, also operative. The latter possibility is outlined in Scheme 7.

It is well established[10,11] that a suitably placed oxygen function will engage in intramolecular coordination with the tin atom of a trialkylstannyl group. Thus, it is highly likely[10,11] that the ester carbonyl oxygen of **8** is coordinated to the *β*-trimethylstannyl group as shown in Scheme 7. Protonation of this substance on the α-carbon rather than on the carbonyl oxygen would lead to the cation **19**. Counterclockwise rotation (least motion[12]) about the C-2−C-3 bond of **19** places the α-Me_3Sn (M in **20**, Scheme 7) in an orientation that allows destannylative regeneration of the double bond to produce, stereoselectively, the *Z* alkenoate **2**.

Scheme 8



Scheme 9



(d) Studies Involving Dimethyl (*Z*,*Z*)- (22), and (*E*,*E*)-2,3,8,9-Tetrakis(trimethylstannyl)-2,8-decadienedioate (24). The synthetic value of the protiodestannylation methods discussed above was demonstrated further by a brief investigation employing the substrates **22** and **24**, which were prepared as outlined in Scheme 8. Pd(0)-catalyzed addition[6] of 2 equiv of hexamethyldistannane to dimethyl 2,8-decadiynedioate (**21**)[6b,13] afforded, in 67% yield, the crystalline *Z*,*Z*-dienedioate **22**. Thermolysis (85 °C, 46 h) of the latter material gave cleanly a mixture of two products. Chromatographic separation of these materials furnished the *Z*,*E* dienedioate **23**, the partially rearranged product, and the corresponding *E*,*E* isomer **24** in yields of 35 and 52%, respectively.

Copper(I) chloride-catalyzed protiodestannylation of **22** produced, after chromatographic purification of the crude product, dimethyl (*E*,*E*)-3,8-bis(trimethylstannyl)-2,8-decadienedioate (**25**) in 65% yield (Scheme 9). On the other hand, treatment of **24** with dilute hydrocloric acid provided, as expected, the *Z*,*Z*-dienedioate **26** (96% yield). Thus, the destannylation methods are applicable to substrates that are structurally more complex than those employed in the initial studies (Tables 1 and 2).

(9) For related mechanistic studies and discussions, see: Cochran, J. C.; Williams, L. E.; Bronk, B. S.; Calhoun, J. A.; Fassberg, J.; Clark, K. G. *Organometallics* **1989**, *8*, 804. Cochran, J. C.; Terrence, K. M.; Phillips, H. K. *Organometallics* **1991**, *10*, 2411.

(10) Jastrzebski, J. T. B. H.; Van Koten, G. *Adv. Organomet. Chem.* **1993**, *35*, 241.

(11) Piers, E.; Coish, P. D. *Synthesis* **1995**, 47 and citations therein.

(12) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; p 782 and citations therein.

(13) We are grateful to Ms. Eva Boehringer for a generous sample of **21**.

Treatment of each of the bis(trimethylstannanes) **25** and **26** with ~5 equiv of CuCl in DMF[14] gave the diesters **27** and **28**, respectively. Clearly, the combination of Pd(0)-catalyzed addition of hexamethyldistannane to α,β-alkynic esters,[6] the new protiodestannylation procedures, and the previously reported[14] copper(I) chloride-mediated intramolecular oxidative coupling of alkenyltrimethylstannane functions provides an easy synthesis of diastereomeric, structurally novel substances such as **27** and **28**.

Conclusion

The studies outlined above resulted in the development of new protocols for the synthesis of alkyl (*E*)- (**1**) and (*Z*)-3-trimethylstannyl-2-alkenoates (**2**), substances that have previously been demonstrated to be valuable synthetic intermediates. Compared with previously described methods for the synthesis of **1** and **2**, involving stereocontrolled reactions of alkyl 2-alkynoates **6** with (trimethylstannyl)cuprate reagents under carefully defined experimental conditions, the protocols disclosed herein offer a number of advantages. Obviously, the new procedures preclude the neccessity of preparing Me_3SnLi and (trimethylstannyl)copper(I) reagents. The preparation of **1** involves two experimentally simple steps, a Pd(0)-catalyzed addition of hexamethyldistannane to alkyl 2-alkynoates **6** and a chemoselective, CuCl-catalyzed protiodestannylation reaction. The sequences leading to **2** (**6** → **7** → **2** or **6** → **7** → **8** → **2**) also employ experimentally straightforward procedures. In fact, all the reactions leading to the production of **1** and **2**, except for **7** → **8**, are carried out at room temperature and, therefore, no low-temperature baths are required. Furthermore, the protiodestannylation steps (**7** → **1** or **2**; **8** → **2**) do not require inert atmospheres and the workup procedures in all of these processes are more convenient than those required for the cuprate-based methods.

Experimental Section

General Experimental Details. Distillation temperatures, which refer to short-path (Kugelrohr) distillations, and melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded by using $CDCl_3$ as the solvent and signal positions (δ values) were measured relative to the signals for $CHCl_3$ (δ 7.24) and $CDCl_3$ (δ 77.0), respectively. Tin−proton coupling constants (J_{Sn-H}) are given as an average of the ^{117}Sn and ^{119}Sn values. GLC was performed on instruments equipped with capillary columns (25 m, HP-5) and flame ionization detectors. TLC was carried out by using commercial aluminum-backed silica gel 60 plates. Flash chromatography[5] was carried out with 230−400 mesh silica gel (E. Merck).

THF was distilled from sodium/benzophenone, while CH_2Cl_2 and *i*-Pr_2NEt were distilled from CaH_2. Commercial DMF (99.9%, Fisher Scientific, Inc.) was used without further purification. Just prior to use, methyl chloroformate, ethyl chloroformate, and chloromethyl methyl ether were passed through a short column of basic alumina (activity I) that had been dried in an oven (~120 °C) overnight and then allowed to cool in a desiccator.

Copper(I) chloride (99.995%+, Aldrich Chemical Co., Inc.) was used without further purification, while tetrakis(triphenylphosphine)palladium(0) was prepared according to the method described by Coulson.[15] Hexamethyldistannane (Organometallics, Inc.) was distilled prior to use.

A solution of 1 N aqueous HCl was prepared by dissolving 83 mL of concentrated HCl (~12 M) in 1 L of water. Aqueous NH_4Cl-NH_4OH (pH ~8) was prepared by the addition of ~50 mL of aqueous NH_3 (30%) to ~950 mL of saturated aqueous NH_4Cl.

All reactions, except those involving the addition of water or aqueous HCl, were carried out under an atmosphere of dry argon using glassware that had been thoroughly flame- and/or oven-dried (~120 °C).

5-(Methoxymethoxy)-1-pentyne. To a cold (0 °C), stirred solution of 4-pentyn-1-ol (3.40 mL, 36.5 mmol) in dry CH_2Cl_2 (70 mL) was added sequentially diisopropylethylamine (9.49 mL, 54.5 mmol) and chloromethyl methyl ether (4.20 mL, 55.3 mmol). After the mixture had been stirred for 1.5 h, 2 N aqueous HCl (70 mL) was added and the resulting mixture was stirred for 15 min. The phases were separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed (brine, 200 mL), dried ($MgSO_4$), and concentrated. Distillation (70−90 °C (35 Torr)) of the crude oil afforded 4.83 g (97%) of the title compound, a colorless oil: IR (neat) 2119, 1150, 1041, 920 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.81 (quintet, 2 H, J = 7 Hz), 1.97 (t, 1 H, J = 1 Hz), 2.33 (dt, 2 H, J = 7, 1 Hz), 3.37 (s, 3 H), 3.64 (t, 2 H, J = 7 Hz), 4.62 (s, 2 H); ^{13}C NMR (50.3 MHz) δ 15.2, 28.5, 55.1, 65.9, 68.5, 83.7, 96.4. HRMS calcd for $C_7H_{12}O_2$ 128.0837, found 128.0838. Anal. Calcd: C, 65.60; H, 9.44. Found: C, 65.40; H, 9.60.

Ethyl 6-(Methoxymethoxy)-2-hexynoate (11). To a cold (−78 °C), stirred solution of 5-(methoxymethoxy)-1-pentyne in dry THF (5 mL) was added a solution of methyllithium in diethyl ether (2.10 mL, 3.02 mmol). The mixture was stirred for 15 min at −78 °C, then warmed to −20 °C, and stirred for 1 h. Ethyl chloroformate (0.30 mL, 3.14 mmol) was added and stirring was continued at −20 °C for 1 h. After the mixture had been warmed to room temperature and stirred for 1 h, saturated aqueous $NaHCO_3$ (5 mL) and diethyl ether (5 mL) were added. The phases were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed (brine, 10 mL), dried ($MgSO_4$), and concentrated. Distillation (95−110 °C (0.6 Torr)) of the crude oil afforded 410 mg (76%) of **11**, a colorless oil: IR (neat) 2236, 1713, 1256, 1040, 753 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.32 (t, 3 H, J = 7 Hz), 1.88 (quintet, 2 H, J = 7 Hz), 2.47 (t, 2 H, J = 7 Hz), 3.36 (s, 3 H), 3.61 (t, 2 H, J = 7 Hz), 4.22 (q, 2H, J = 7 Hz), 4.61 (s, 2 H); ^{13}C NMR (50.3 MHz) δ 14.0, 15.5, 27.7, 55.2, 61.7, 65.7, 73.4, 88.3, 96.4, 153.7. HRMS calcd for $C_{10}H_{15}O_4$ ($M^+ - H$) 199.0971, found 199.0966. Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.08. Found: C, 59.76; H, 8.17.

Ethyl (*Z*)-6-(Methoxymethoxy)-2,3-bis(trimethylstannyl)-2-hexenoate (7e). To a stirred solution of ethyl 6-(methoxymethoxy)-2-hexynoate (**11**) (1.08 g, 5.41 mmol) in dry THF (40 mL) was added sequentially hexamethyldistannane (1.12 mL, 5.41 mmol) and $[Ph_3Pd]_4Pd$ (63 mg, 0.054 mmol). The mixture was heated to reflux for 8 h and then was concentrated under reduced pressure. Flash chromatography (100 g of silica gel, 10:1 pentane−Et_2O) of the crude oil afforded 2.53 g (89%) of **7e**, a colorless oil: IR (neat) 1703, 1186, 1038, 771, 526 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.209 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 0.212 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 1.26 (t, 3 H, J = 7 Hz), 1.59−1.67 (m, 2 H), 2.36−2.42 (m, 2 H), 3.31 (s, 3 H), 3.47 (t, 2 H, J = 7 Hz), 4.13 (q, 2 H, J = 7 Hz), 4.56 (s, 2 H); ^{13}C NMR (50.3 MHz) δ −6.7, 14.5, 30.2, 37.4, 55.1, 60.1, 67.3, 96.3, 149.9, 164.2, 171.7. HRMS calcd for $C_{15}H_{31}O_4{}^{120}Sn_2$ ($M^+ - Me$) 515.0266, found 515.0255. Anal. Calcd for $C_{16}H_{34}O_4Sn_2$: C, 36.41; H, 6.49. Found: C, 36.51; H, 6.49.

Methyl (*Z*)-3-Phenyl-2,3-bis(trimethylstannyl)propenoate (7f). To a stirred solution of methyl 3-phenylpropynoate (**12**) (1.00 g, 6.25 mmol) in dry THF (50 mL) was added sequentially hexamethylditin (1.05 mL, 6.25 mmol) and $[Ph_3Pd]_4Pd$ (72 mg, 0.063 mmol). The mixture was heated to reflux for 2 h and then was concentrated under reduced pressure. Flash chromatography (100 g of silica gel, 95:5 pentane−Et_2O) of the crude oil afforded 2.05 g (67%) of **7f**, a crystalline solid: mp 78−79 °C; IR (KBr) 3056, 2987, 1714, 1595, 1429, 1219, 1016, 773 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.11 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.29 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 3.35 (s, 3 H), 6.89 (dm, 2 H, J = 8 Hz), 7.08 (tt, 1 H, J = 7, 1 Hz), 7.17−7.27 (m, 2 H); ^{13}C NMR (75 MHz) δ −6.7, −6.6, 50.8,

(14) Piers, E.; Romero, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 1215.
(15) Coulson, D. R. *Inorganic Synthesis* **1972**, *13*, 121.

125.2, 125.6, 128.0, 147.0, 152.3, 165.6, 172.1. HRMS calcd for $C_{15}H_{23}O_2{}^{120}Sn_2$ ($M^+ - Me$) 474.9742, found 474.9734. Anal. Calcd for $C_{16}H_{26}O_2Sn_2$: C, 39.40; H, 5.37. Found: C, 39.62; H, 5.36.

Methyl (*Z*)-2,3-Bis(trimethylstannyl)-2-octenoate (7g). To a stirred solution of methyl 2-octynoate (**13**) (1.00 g, 6.49 mmol) in dry THF (40 mL) was added sequentially hexamethylditin (1.1 mL, 6.49 mmol) and $[Ph_3Pd]_4Pd$ (75 mg, 0.065 mmol). The resulting mixture was heated to reflux for 3 h and then was concentrated under reduced pressure. Flash chromatography (100 g of silica gel, 98:2 pentane−Et_2O) of the crude oil afforded 2.14 g (68%) of **7g**, a colorless oil: IR (neat) 2930, 2859, 1712, 1433, 1256, 1191, 771 cm^{-1}; ^1H NMR (400 MHz) δ 0.19 (s, 9 H, $^2J_{Sn-H} = 60$ Hz), 0.21 (s, 9 H, $^2J_{Sn-H} = 58$ Hz), 0.86 (t, 3 H, $J = 7$ Hz), 1.20−1.40 (m, 6 H), 2.29 (t, 2 H, $J = 7$ Hz, $^3J_{Sn-H} = 58$ Hz), 3.67 (s, 3 H); ^{13}C NMR (75 MHz) δ −6.8, −6.7, 14.0, 22.5, 29.8, 31.7, 41.1, 51.0, 148.6, 165.6, 172.4. HRMS calcd for $C_{14}H_{29}O_2{}^{120}Sn_2$ ($M^+ - Me$) 469.0212, found 469.0214.

Methyl (*E*)-3-Phenyl-2,3-bis(trimethylstannyl)propenoate (8f). Neat methyl (*Z*)-3-phenyl-2,3-bis(trimethylstannyl)propenoate (**7f**) (0.50 g, 1.03 mmol) was heated (85 °C) under an argon atmosphere for 26 h. Flash chromatography (50 g of silica gel, 98:2 pentane−Et_2O) of the crude oil afforded 0.42 g (84%) of **8f**, a crystalline solid: mp 56−57 °C; IR (KBr) 3058, 2981, 2914, 1695, 1552, 1486, 1434, 1236, 1206, 1033, 772 cm^{-1}; ^1H NMR (400 MHz) δ −0.16 (s, 9 H, $^2J_{Sn-H} = 55$ Hz), 0.03 (s, 9 H, $^2J_{Sn-H} = 54$ Hz), 3.76 (s, 3 H), 6.85 (dm, 2 H, $J = 8$ Hz), 7.15 (tt, 1 H, $J = 8$, 1 Hz), 7.26 (tm, 2 H), $J = 8$ Hz); ^{13}C NMR (75 MHz) δ −6.9, −6.6, 51.9, 125.5, 126.1, 128.1, 128.2, 147.8, 172.3, 182.2. HRMS calcd for $C_{15}H_{23}O_2{}^{118}Sn{}^{120}Sn$ ($M^+ - Me$) 472.9736, found 472.9732. Anal. Calcd for $C_{16}H_{26}O_2Sn_2$: C, 39.40; H, 5.37. Found: C, 39.70; H, 5.41.

General Procedure 1. CuCl-Catalyzed Protiodestannylation of the Alkyl (*Z*)-2,3-Bis(trimethylstannyl)-2-alkenoates 7a−g. Preparation of the Alkyl (*E*)-3-Trimethylstannyl-2-alkenoates 1a−g. To a stirred solution of the substrate **7** in DMF were added water and solid CuCl. The resulting pale green solution was stirred at room temperature for the specified length of time and then aqueous NH_4Cl−NH_4OH (pH ∼8, one-quarter of the volume of DMF) and diethyl ether (one-quarter of the volume of DMF) were added. The mixture was stirred, open to the atmosphere, for 10 min. The phases were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed sequentially with water and brine and then were dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography on silica gel.

The quantities of materials used for the individual experiments and the isolated yields of the products are summarized in Table 1. Of the products **1a**−**g** prepared via this general procedure, substances **1a**,[3c] **1b**,[3c] and **1d**[3e] were reported previously. The following new alkyl (*E*)-3-trimethylstannyl-2-alkenoates were prepared.

Ethyl (*E*)-5-chloro-3-trimethylstannyl-2-pentenoate (1c) was obtained as a colorless oil: IR (neat) 1713, 1599, 1185, 1034, 773 cm^{-1}; ^1H NMR (400 MHz) δ 0.21 (s, 9 H, $^2J_{Sn-H} = 54$ Hz), 1.27 (t, 3 H, $J = 7$ Hz), 3.28 (dt, 2 H, $J = 1$, 7 Hz, $^3J_{Sn-H} = 55$ Hz), 3.60 (t, 2 H, $J = 7$ Hz), 4.14 (q, 2 H, $J = 7$ Hz), 6.07 (t, 1 H, $J = 1$ Hz, $^3J_{Sn-H} = 69$ Hz); ^{13}C NMR (50.3 MHz) δ −8.8, 14.3, 37.1, 43.7, 59.9, 130.7, 163.8, 168.2. HRMS calcd for $C_9H_{16}{}^{35}ClO_2{}^{120}Sn$ ($M^+ - Me$) 310.9861, found 310.9854. Anal. Calcd for $C_{10}H_{19}ClO_2Sn$: C, 36.91; H, 5.89. Found: C, 36.98; H, 5.93.

Ethyl (*E*)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (1e), a colorless oil, exhibited IR (neat) 1714, 1598, 1368, 1175, 1043, 773 cm^{-1}; ^1H NMR (400 MHz) δ 0.21 (s, 9 H, $^2J_{Sn-H} = 55$ Hz), 1.29 (t, 3 H, $J = 7$ Hz), 1.68−1.77 (m, 2 H), 2.96 (dt, 2 H, $J = 1$, 7 Hz, $^3J_{Sn-H} = 52$ Hz), 3.37 (s, 3H), 3.55 (t, 2 H, $J = 7$ Hz), 4.17 (q, 2 H, $J = 7$ Hz), 4.62 (s, 2 H), 5.98 (t, 1 H, $J = 1$ Hz, $^3J_{Sn-H} = 73$ Hz); ^{13}C NMR (50.3 MHz) δ −9.1, 14.3, 29.7, 31.5, 55.1, 59.7, 67.6, 96.4, 128.0, 164.2, 172.2. HRMS calcd for $C_{12}H_{23}O_4{}^{120}Sn$ ($M^+ - Me$) 351.0618, found 351.0618. Anal. Calcd for $C_{13}H_{26}O_4Sn$: C, 42.77; H, 7.18. Found: C, 42.66; H, 7.24.

Methyl (*E*)-3-Phenyl-3-trimethylstannylpropenoate (1f). This material is a colorless oil: IR (neat) 2950, 1731, 1605, 1434, 1165, 1073, 834 cm^{-1}; ^1H NMR (400 MHz) δ 0.19 (s, 9 H, $^2J_{Sn-H} = 52$ Hz), 3.53 (s, 3 H), 6.14 (s, 1 H, $^3J_{Sn-H} = 66$ Hz), 6.93 (dm, 2 H, $J = 8$ Hz), 7.16 (tt, 1 H, $J = 7$, 1 Hz), 7.29 (tm, 2 H, $J = 8$ Hz); ^{13}C NMR (75 MHz) δ −9.2, 51.0, 124.6, 125.8, 127.5, 128.0, 143.8, 164.6, 168.9. HRMS calcd for $C_{12}H_{15}O_2{}^{120}Sn$ ($M^+ - Me$) 311.0094, found 311.0086.

Methyl (*E*)-3-trimethylstannyl-2-octenoate (1g,) a colorless oil, displayed IR (neat) 2958, 2859, 1721, 1596, 1434, 1256, 1169, 771 cm^{-1}; ^1H NMR (400 MHz) δ 0.17 (s, 9 H, $^2J_{Sn-H} = 53$ Hz), 0.80−0.95 (m, 3 H), 1.22−1.45 (m, 6 H), 2.86 (td, 2 H, $J = 1$, 8 Hz, $^3J_{Sn-H} = 62$ Hz), 3.68 (s, 3 H), 5.94 (br s, 1 H, $^3J_{Sn-H} = 74$ Hz); ^{13}C NMR (75 MHz) δ −9.1, 14.0, 22.5, 29.3, 31.8, 34.7, 50.8, 126.8, 164.7, 174.1. HRMS calcd for $C_{11}H_{21}O_2{}^{120}Sn$ ($M^+ - Me$) 305.0564, found 305.0554. Anal. Calcd for: $C_{12}H_{24}O_2Sn$: C, 45.18; H, 7.58. Found: C, 45.51; H, 7.73.

General Procedure 2. Hydrochloric Acid-Mediated Protiodestannylation of the Alkyl (*Z*)- and (*E*)-2,3-Bis(trimethylstannyl)-2-alkenoates (7a−f, 8a−f, Respectively). Preparation of the Alkyl (*Z*)-3-Trimethylstannyl-2-alkenoates 2a−f. To a stirred solution of the alkyl 2,3-bis(trimethylstannyl)-2-alkenoate **7** or **8** in DMF was added 1 N hydrochloric acid. The mixture was stirred at room temperature for the specified length of time and then saturated aqueous $NaHCO_3$ (one-quarter the volume of DMF) and diethyl ether (one-quarter the volume of DMF) were added. The phases were separated and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography on silica gel.

The quantities of materials used for the individual experiments, the reaction times, and the isolated yields of the products are summarized in Table 2. Of the products **2a**−**f** prepared via this general procedure, substances **2a**,[3c] **2b**,[3c] and **2d**[3e] were reported previously. The following new alkyl (*Z*)-3-trimethylstannyl-2-alkenoates were prepared.

Ethyl (*Z*)-5-chloro-3-trimethylstannyl-2-pentenoate (2c), a colorless oil, exhibited IR (neat) 1704, 1603, 1207, 774 cm^{-1}; ^1H NMR (400 MHz) δ 0.17 (s, 9 H, $^2J_{Sn-H} = 55$ Hz), 1.26 (t, 3 H, $J = 7$ Hz), 2.84 (dt, 2 H, $J = 1$, 7 Hz, $^3J_{Sn-H} = 43$ Hz), 3.53 (t, 2 H, $J = 7$ Hz), 4.17 (q, 2 H, $J = 7$ Hz), 6.39 (t, 1 H, $J = 1$ Hz, $^3J_{Sn-H} = 114$ Hz); ^{13}C NMR (50.3 MHz) δ −7.3, 14.2, 41.9, 42.9, 60.5, 130.5, 167.6, 170.1. HRMS calcd for $C_9H_{16}{}^{35}ClO_2{}^{120}Sn$ ($M^+ - Me$) 310.9861, found 310.9866. Anal. Calcd for $C_{10}H_{19}ClO_2Sn$: C, 36.91; H, 5.89. Found: C, 37.00; H, 5.98.

Ethyl (*Z*)-6-methoxymethoxy-3-trimethylstannyl-2-hexenoate (2e) was obtained as a colorless oil: IR (neat) 1703, 1600, 1325, 1207, 1041, 774 cm^{-1}; ^1H NMR (400 MHz) δ 0.14 (s, 9 H, $^2J_{Sn-H} = 54$ Hz), 1.25 (t, 3 H, $J = 7$ Hz), 1.62−1.71 (m, 2 H), 2.48 (dt, 2 H, $J = 1$, 8 Hz, $^3J_{Sn-H} = 47$ Hz), 3.32 (s, 3 H), 3.48 (t, 2 H, $J = 7$ Hz), 4.15 (q, 2 H, $J = 7$ Hz), 4.57 (s, 2 H), 6.34 (t, 1 H, $J = 1$ Hz, $^3J_{Sn-H} = 119$ Hz); ^{13}C NMR (50.3 MHz) δ −7.4, 14.3, 29.1, 36.5, 55.1, 60.3, 66.9, 96.4, 128.3, 167.9, 174.8. HRMS calcd for $C_{12}H_{23}O_4{}^{120}Sn$ ($M^+ - Me$) 351.0614, found 351.0618. Anal. Calcd for $C_{13}H_{26}O_4Sn$: C, 42.77; H, 7.18. Found: C, 42.87; H, 7.24.

Methyl (*Z*)-3-phenyl-3-trimethylstannylpropenoate (2f), a colorless crystalline solid (mp 28−29 °C), displayed IR (KBr) 1709, 1587, 1319, 1178, 1017, 769 cm^{-1}; ^1H NMR (400 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H} = 55$ Hz), 3.78 (s, 3 H), 6.48 (s, 1 H, $^3J_{Sn-H} = 107$ Hz), 7.04−7.09 (m, 2 H), 7.20−7.27 (m, 1 H), 7.28−7.35 (m, 2 H); ^{13}C NMR (50.3 MHz) δ −6.3, 51.7, 126.5, 127.1, 128.1, 129.8, 144.8, 168.2, 173.6. HRMS calcd for $C_{12}H_{15}O_2{}^{120}Sn$ ($M^+ - Me$) 311.0094, found 311.0085. Anal. Calcd for $C_{13}H_{18}O_2Sn$: C, 48.05; H, 5.58. Found: C, 47.82; H, 5.68.

Dimethyl (*Z*,*Z*)-2,3,8,9-Tetrakis(trimethylstannyl)-2,8-decadienedioate (22). To a stirred solution of dimethyl 2,8-decadiynedioate (**21**)[6b] (0.352 g, 1.59 mmol) in dry THF (15 mL) was added sequentially $Me_3SnSnMe_3$ (535 μL, 3.17 mmol) and $(Ph_3P)_4Pd$ (55 mg, 0.045 mmol). The mixture was refluxed for 3 h and then was concentrated under reduced pressure. Flash chromatography (50 g of silica gel, 95:5 pentane−Et_2O) of the crude oil afforded 0.916 g (67%) of the title compound,

a colorless crystalline solid: mp 54−55 °C; IR (KBr) 2984, 2919, 1708, 1551, 1430, 1191, 1024, 771 cm^{-1}; ^1H NMR (400 MHz) δ 0.20 (s, 18 H, $^2J_{Sn-H}$ = 52 Hz), 0.21 (s, 18 H, $^2J_{Sn-H}$ = 54 Hz), 1.25−1.40 (m, 4 H), 2.29 (t, 4 H, J = 7 Hz, $^3J_{Sn-H}$ = 57 Hz), 3.68 (s, 6 H); ^{13}C NMR (75 MHz) δ −6.8, −6.6, 30.2, 40.9, 51.0, 149.0, 165.0, 172.3. HRMS calcd for $C_{17}H_{29}O_4{}^{118}Sn^{120}Sn$ ($M^+ - Me_7Sn_2$) 535.0104, found 535.0114. Anal. Calcd for $C_{24}H_{50}O_4Sn_4$: C, 32.85; H, 5.74. Found: C, 33.19; H, 6.05.

Dimethyl (*Z*,*E*)- (23) and (*E*,*E*)-2,3,8,9-Tetrakis(trimethylstannyl)-2,8-decadienedioate (24). Neat **22** (0.50 g, 0.58 mmol) was heated (85 °C) under an argon atmosphere for 46 h. Flash chromatography (50 g of silica gel, 95:5 pentane−Et_2O) of the crude oil afforded (in order of elution) 0.259 g (52%) of the *E*,*E* dienedioate **24**, a crystalline substance (colorless plates, mp 139−140 °C), and 0.174 g (35%) of the *Z*,*E* dienoate (**23**), a colorless oil.

Compound **24**: IR (KBr) 2987, 2926, 1714, 1691, 1431, 1235, 751 cm^{-1}; ^1H NMR (400 MHz) δ 0.13 (s, 18 H, $^2J_{Sn-H}$ = 53 Hz), 0.22 (s, 18 H, $^2J_{Sn-H}$ = 54 Hz), 1.25−1.40 (br m, 4H), 2.40−2.50 (br m, 4 H, $^3J_{Sn-H}$ = 58 Hz), 3.69 (s, 6 H); ^{13}C NMR (75 MHz) δ −6.5, −5.9, 30.5, 41.4, 51.8, 144.1, 172.1, 183.9. HRMS calcd for $C_{23}H_{47}O_4{}^{120}Sn_4$ (M^+ − Me) 866.9562, found 866.9549. Anal. Calcd for $C_{24}H_{50}O_4Sn_4$: C, 32.85; H, 5.74. Found: C, 33.22; H, 6.03.

Compound **23**: IR (neat) 2986, 2919, 1708, 1693, 1547, 1432, 1226, 1024, 774 cm^{-1}; ^1H NMR (400 MHz) δ 0.12 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.20 (s, 9 H, $^2J_{Sn-H}$ = 52 Hz), 0.21 (s, 18 H, $^2J_{Sn-H}$ = 54 Hz), 1.20−1.31 (m, 2 H), 1.32−1.45 (m, 2 H), 2.28−2.36 (m, 2 H), 2.37−2.48 (m, 2 H), 3.66 (s, 3 H), 3.67(s, 3 H); ^{13}C NMR (75 MHz) δ −6.8, −6.6, −6.5, −6.0, 30.3, 30.4, 40.8, 41.6, 51.0, 51.8, 143.8, 149.3, 164.5, 172.1, 172.3, 184.3. HRMS calcd for $C_{24}H_{50}O_4{}^{120}Sn_4$ 866.9562, found 866.9529. Anal. Calcd for $C_{24}H_{50}O_4Sn_4$: C, 32.85; H, 5.74. Found: C, 33.22; H, 5.99.

Dimethyl (*E*,*E*)-3,8-Bis(trimethylstannyl)-2,8-decadienedioate (25). Following general procedure 1 (vide supra), the *Z*,*Z* dienedioate **22** was converted into the title compound **25** with the following quantities of reagents and solvents: **22** (210 mg, 0.243 mmol), CuCl (0.4 mg, 0.004 mmol), DMF (5 mL), and water (0.5 mL). Flash chromatography (30 g of silica gel, 9:1 petroleum ether−Et_2O) of the crude oil afforded 88 mg (65%) of **25**, a colorless oil: IR (neat) 2948, 2856, 1719, 1595, 1433, 1352, 1155, 771 cm^{-1}; ^1H NMR (400 MHz) δ 0.18 (s, 18 H, $^2J_{Sn-H}$ = 54 Hz), 1.40−1.50 (m, 4 H), 2.79−3.10 (m, 4 H, $^3J_{Sn-H}$ = 62 Hz), 3.69 (s, 6 H), 5.94 (t, 2 H, J = 1 Hz, $^3J_{Sn-H}$ = 74 Hz). HRMS calcd for $C_{17}H_{31}O_4{}^{120}Sn_2$ (M^+ − Me) 539.0266, found 539.0261. Anal. Calcd for $C_{18}H_{34}O_4Sn_2$: C, 38.99; H, 6.00. Found: C, 39.26; H, 6.00.

Dimethyl (*Z*,*Z*)-3,8-Bis(trimethylstannyl)-2,8-decadienedioate (26). Following general procedure 2 (vide supra), substrate **24** was converted into **26** with the following quantities of reagents and solvents: **24** (131 mg, 0.151 mmol), 1 N hydrochloric acid (0.36 mL), and DMF (3 mL). The reaction temperature was 70 °C and the reaction time in this case was 1 h. Flash chromatography (30 g of silica gel, 95:5 petroleum ether−Et_2O) of the crude oil afforded 81 mg (96%) of the *Z*,*Z* dienedioate **26**, a colorless crystalline (mp 75−77 °C) material: IR (KBr) 2930, 2856, 1709, 1600, 1436, 1210, 1045, 773 cm^{-1}; ^1H NMR (400 MHz) δ 0.15 (s, 18 H, $^2J_{Sn-H}$ = 54 Hz), 1.30−1.48 (m, 4 H), 2.40 (t, 4 H, J = 7 Hz, $^3J_{Sn-H}$ = 48 Hz), 3.70 (s, 6 H), 6.32 (s, 2 H, $^3J_{Sn-H}$ = 119 Hz); ^{13}C NMR (75 MHz) δ 7.4, 28.8, 39.8, 51.5, 127.7, 168.3, 175.7. HRMS calcd for $C_{17}H_{31}O_4{}^{120}Sn_2$ (M^+ − Me) 539.0266, found 539.0244.

(*E*,*E*)-1,2-Bis(methoxycarbonylmethylidene)cyclohexane (27). To a warm (60 °C), stirred slurry of CuCl (0.063 g, 0.64 mmol) in 2 mL of DMF was added a solution of the *E*,*E* dienedioate **25** (0.071 g, 0.13 mmol) in 1 mL of DMF. After the reaction mixture had been stirred for 15 min, it was allowed to cool to room temperature. Aqueous NH_4Cl-NH_4OH (pH ∼8, 3 mL) and water (5 mL) were added sequentially to the vigorously stirred mixture, which was then extracted with Et_2O (3 × 25 mL). The combined organic extracts were washed (water, 3 × 25 mL; brine, 25 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (30 g of silica gel, 9:1 petroleum ether−Et_2O) of the remaining oil afforded 19 mg (66%) of **27**, a colorless crystalline substance: mp 32−33 °C; IR (KBr) 1719, 1635, 1435, 1173, 870 cm^{-1}; ^1H NMR (400 MHz) δ 1.69−1.73 (m, 4 H), 2.92−2.99 (m, 4 H), 3.69 (s, 6 H), 5.81 (s, 2 H); ^{13}C NMR (50.3 MHz) δ 25.7, 30.1, 51.2, 114.6, 160.5, 166.6. HRMS calcd for $C_{12}H_{16}O_4$ 224.1049, found 224.1058. Anal. Calcd: C, 64.27; H, 7.19. Found: C, 64.12; H, 7.15.

(*Z*,*Z*)-1,2-Bis(methoxycarbonylmethylidene)cyclohexane (28). To a warm (60 °C), stirred slurry of CuCl (0.048 g, 0.48 mmol) in 2 mL of DMF was added a solution of the *Z*,*Z* dienedioate **26** (53 mg, 0.096 mmol) in 0.5 mL of DMF. The reaction mixture was stirred for 35 min, was allowed to cool to room temperature, and then, while being stirred vigorously, was treated sequentially with aqueous NH_4Cl-NH_4OH (pH ∼8, 3 mL) and water (5 mL). The mixture was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed (water, 3 × 20 mL; brine, 20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (30 g of silica gel, 9:1 petroleum ether−Et_2O) of the crude product gave 14 mg (65%) of the title diester **28**, a colorless crystalline material: mp 60 °C (dec); IR (KBr) 2947, 2859, 1730, 1665, 1637, 1439, 1336, 1283, 1171, 1021, 851 cm^{-1}; ^1H NMR (400 MHz) δ 1.50−1.68 (m, 2 H), 1.86−2.10 (br unresolved m, 2 H), 2.22−2.40 (br unresolved m, 2 H), 2.51 (br d, 2 H, J = 12 Hz), 3.60 (s, 6 H), 5.73 (s, 2 H). In a NOE experiment, irradiation of the singlet at δ 5.73 (vinylic proton) enhances the broad doublet at 2.51 and the broad multiplet at 2.22−2.40; ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.2, 40.0, 51.1, 113.8, 157.0, 166.1. HRMS calcd for $C_{12}H_{16}O_4$ 224.1049, found 224.1054. Anal. Calcd: C, 64.27; H, 7.19. Found: C, 64.12; H, 7.24.

Acknowledgment. We gratefully acknowledge the Natural Sciences and Engineering Research Council of Canada for financial support and for a Postgraduate Scholarship (to E.J.M.), Merck Frosst Canada Inc. for financial assistance, and Bio-Méga/Boehringer Ingelheim Research Inc. for a Scholarship (to E.J.M.).

JO9707693