standard parameters. Optimized structures were determined by minimizing the energy with respect to all geometrical parameters without imposing molecular symmetry constraints.

Supplementary Material Available: Tables comparing experimental and MM2 calculated structural features (2 pages). Ordering information is given on any current masthead page.

(29) (a) Stewart, J. J. P. *QCPE Bull.* **1983**, *3*, 101. (b) Olivella, S. *QCPE Bull.* **1984**, *4*, 109.

Dilithium (Trimethylstannyl)(2-thienyl)(cyano)cuprate, a Synthetically Useful Higher Order Cuprate Reagent

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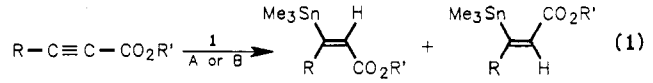
Recently, we described, inter alia, the preparation of lithium (trimethylstannyl)(phenylthio)cuprate (**1**) and showed that this lower order cuprate reagent readily transfers the Me_3Sn moiety to the β carbon of a variety of α,β-unsaturated carbonyl compounds.[1] Subsequently,

$$[Me_3SnCuSPh]Li$$
1

it was shown that **1** can be used effectively for the conversion of α,β-acetylenic esters **2** into either alkyl (*E*)- or (*Z*)-3-(trimethylstannyl)-2-alkenoates (**3**, **4**, respectively).[2] Thus, treatment of substrates **2** with reagent **1** in tetrahydrofuran (THF) at −78 °C in the presence of methanol (conditions A, eq 1) provides, stereoselectively, the *E*

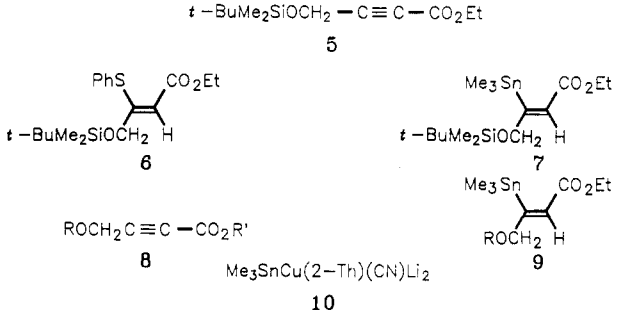


(1)

	2	**3**		**4**
A: THF, MeOH, −78°C		≥96	:	≤ 4
B: THF, −48°C; MeOH		≤ 7	:	≥93

products **3**, while reaction of **2** with **1** under conditions B, eq 1, gives largely the *Z* products **4**.[2a,c] Interestingly, of the various (trimethylstannyl)copper(I) reagents employed thus far in our work,[1,2] a number of them may be used for the stereoselective transformation of **2** into **3**,[2] while only **1** effects the efficient, stereocontrolled conversion of **2** into **4**.[2a,c]

It was found, however, that the reactions of **1** with α,β-acetylenic esters containing an ether function on the γ carbon were anomalous. For example, reaction of **1** with **5** under conditions B outlined in eq 1 gave **6** as the major product (35%).[2b,c] The expected, desired product **7** was produced in only 29% yield.[2b,c] The preferred transfer of the phenylthio group was also observed in the reaction of reagent **1** with other α,β-acetylenic esters of general structure **8**. Since, in connection with other research projects, we required compounds of general structure **9**, we were interested in finding a (trimethylstannyl)copper(I) reagent that would convert **8** into **9** in a clean, efficient manner.



Although intermediates derived from the interaction of various (trimethylstannyl)copper(I) reagents with α,β-acetylenic esters **1** are readily protonated to afford **3** and/or **4** (eq 1), we[3] and others[4] have shown that these intermediates cannot be trapped with electrophiles other than a proton. Consequently, another goal of the present work was to search for a reagent that, upon transfer of the Me_3Sn group to the β carbon of substrates **1**, would produce intermediates that would be amenable to reaction with other electrophiles, particularly alkylating agents.

Important recent work in organocopper chemistry has shown that higher order alkyl, alkenyl, and aryl cuprates are readily prepared and possess very useful chemical reactivity.[5] In many instances, these reagents are synthetically superior to the corresponding lower order cuprates. Consequently, it seemed worthwhile to investigate the possibility that a higher order (trimethylstannyl)cuprate might serve our purposes in connection with the problems outlined above. We summarize herein the results of a brief study on the synthesis and chemistry of one such reagent, dilithium (trimethylstannyl)(2-thienyl)(cyano)cuprate (**10**).[6]

Results and Discussion

(a) Preparation of Reagent 10. A convenient method for preparing the higher order cuprate **10** involved the following procedure. Ethereal MeLi (2 equiv) was added to a THF solution (−20 °C) of a mixture of $(Me_3Sn)_2$ (1 equiv) and thiophene (1 equiv). After the solution had been stirred at −20 °C for 50 min, it was cooled to −78 °C and solid CuCN (1 equiv) was added. Warming of the resultant suspension to −48 °C afforded a bright yellow solution of reagent **10**, which was used immediately.

(b) Reaction of 10 with α,β-Unsaturated Carbonyl Compounds. In order to acquire information regarding the chemical reactivity of reagent **10**, its reaction with a number of α,β-unsaturated carbonyl compounds was carried out. Treatment of the enones **11** and **12** with 1.5 equiv of **10** in THF at −20 °C gave the corresponding conjugate addition products **18** (90%) and **19**[1b] (87%), respectively. A similar reaction involving (*R*)-(+)-pulegone (**13**) afforded

(1) (a) Piers, E.; Morton, H. E. *J. Chem. Soc., Chem. Commun.* **1978**, 1034. (b) Piers, E.; Morton, H. E.; Chong, J. M. *Can. J. Chem.* **1987**, *78*, 65.

(2) (a) Piers, E.; Morton, H. E. *J. Org. Chem.* **1980**, *45*, 4263. (b) Piers, E.; Chong, J. M.; Morton, H. E. *Tetrahedron Lett.* **1981**, *49*, 4905. (c) Piers, E.; Chong, J. M.; Morton, H. E., submitted for publication in *Tetrahedron*.

(3) Piers, E.; Chong, J. M. *J. Org. Chem.* **1982**, *47*, 1602.

(4) Cox, S. D.; Wudl, F. *Organometallics* **1983**, *2*, 184.

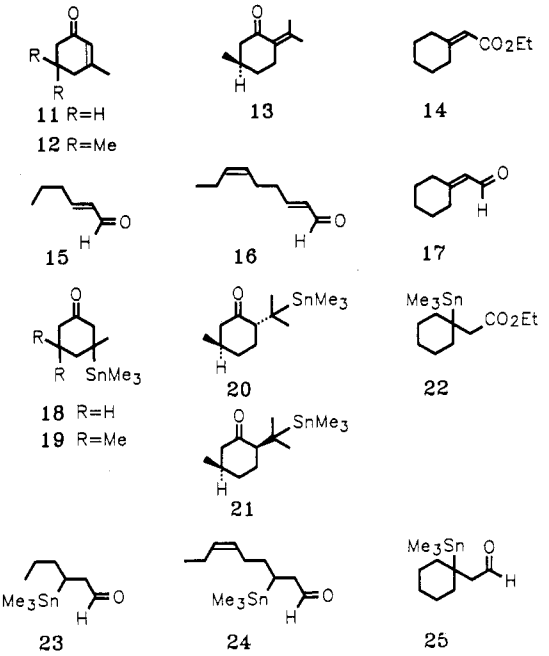
(5) (a) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *24*, 5005. (b) Lipshutz, B. H. *Synthesis* **1987**, 325.

(6) 2-Th refers to the 2-thienyl group. This moiety has been shown to be an excellent nontransferable ligand for mixed organocuprates and has been employed by Lipshutz and co-workers[5,7] in the preparation of versatile higher order cuprates. The formulation shown in **10** is not meant to represent an actual structure, but is used for convenience and to show stoichiometry. Analogous formulations have been used for higher order alkylcuprates.[5,7]

(7) Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945.

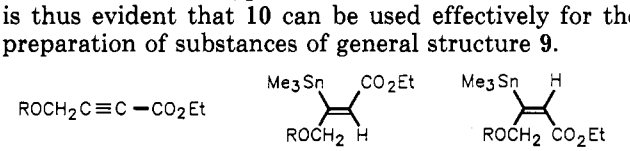
0022-3263/88/1953-5366$01.50/0

a high yield of a 3:1 mixture of the epimers **20** and **21**, which could be separated by flash chromatography[8] on silica gel. The stereochemistry of **20** and **21** was shown by the fact that the cis compound **21**, upon treatment with sodium methoxide in methanol, produced a 12:88 mixture of **21** and the more stable trans isomer **20**, respectively.



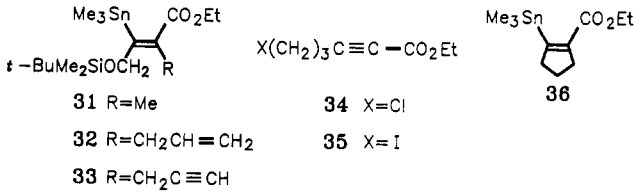
The higher order cuprate **10** also effected smooth conjugate transfer of the Me_3Sn group to α,β-unsaturated esters and aldehydes. For example, the substrates **14–17** were readily transformed into the corresponding products **22–25**, respectively. The conversion of **14** into **22** is of particular note, since it had been shown previously[1] that this transformation was unsuccessful when the lower order cuprate **1** was employed as the reagent. On the other hand, upon reaction with Me_3SnLi, substrate **14** is converted into **22** under conditions much milder[9] than those required for reagent **10**. Thus, in conjugate addition reactions, the higher order cuprate **10** is less reactive than the "parent" reagent Me_3SnLi but is more reactive than the lower order cuprate **1**.

(c) Reaction of 10 with α,β-Acetylenic Esters. Our experiments in this area showed that the two primary objectives of the present study (vide supra) could be achieved by use of reagent **10**. Reaction (THF, −78 °C, 2 h) of the α,β-acetylenic ester **5**[2b,c] with the higher order cuprate **10** afforded a 95:5 mixture of the geometric isomers **27**[2b,c] and **29**,[2b,c] respectively. Flash chromatography[8] of this mixture provided the *Z* isomer **27**[2b,c] in 65% yield. In similar fashion, treatment of the substrate **26** with reagent **10**, followed by flash chromatography[8] of the resultant 9:1 mixture of **28** and **30**, provided the *Z* isomer **28** (55%). It is thus evident that **10** can be used effectively for the preparation of substances of general structure **9**.



5 R= *t*-BuMe$_2$Si **27** R= *t*-BuMe$_2$Si **29** R= *t*-BuMe$_2$Si
26 R= MeOCH$_2$ **28** R= MeOCH$_2$ **30** R= MeOCH$_2$

Interestingly, the intermediate derived from the interaction of **5** with **10** can be trapped with reactive alkylating agents.[10] For example, treatment of the α,β-acetylenic ester **5** with reagent **10**, followed by successive addition of hexamethylphosphoramide (HMPA) and methyl iodide, afforded a single product that was isolated in 65% yield and was shown to be ethyl (*Z*)-4-(*tert*-butyldimethylsiloxy)-2-methyl-3-(trimethylstannyl)-2-butenoate (**31**). Similarly, use of 3-iodopropene and 3-bromopropyne as alkylating agents provided the tetrasubstituted alkenes **32** (60%) and **33** (40%), respectively. In the experiment involving the use of 3-bromopropyne, product **33** was accompanied by a significant amount of a mixture of the products **27** and **29**, resulting from protonation of the intermediate.



31 R=Me **34** X=Cl
32 R=$CH_2CH{=}CH_2$ **35** X=I
33 R=$CH_2C{\equiv}CH$

The stereochemistry of the alkylation products **31–33** was confirmed by appropriate nuclear Overhauser enhancement difference (NOED) experiments. For example, in the ^1H NMR spectrum of **31**, irradiation at δ 1.93 (vinyl Me group) caused enhancement of the signal at δ 4.40 (*t*-BuMe$_2$SiOCH_2). Similar experiments involving compounds **32** and **33** showed conclusively that these substances possessed the indicated stereochemistry.

When a suitable ω-halo α,β-acetylenic ester is allowed to react with reagent **10**, conjugate addition–intramolecular alkylation is observed. For example, reaction (THF, −78 °C, 2 h; −48 °C, 1 h) of ethyl 6-iodo-2-hexynoate (**35**) with **10**, followed by flash chromatography[8] of the crude product, afforded ethyl 2-(trimethylstannyl)-1-cyclopentenecarboxylate (**36**) (62%).

In summary, it has been shown that the new higher order (trimethylstannyl)cuprate **10** is a viable reagent for the conjugate transfer of the Me_3Sn group to a variety of α,β-unsaturated carbonyl compounds and the α,β-acetylenic esters **5** and **26**. With the latter substrates, protonation of the intermediates provides, stereoselectively, the corresponding alkyl (*Z*)-3-(trimethylstannyl)-2-alkenoates **27** and **28**, respectively. The intermediate derived from substrate **5** can be alkylated with highly reactive alkylating agents.

Experimental Section

General Procedures. Distillation temperatures are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 1710 spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ solutions. Signal positions are given in ppm (δ) and were measured relative to the signal for $CHCl_3$ (δ 7.25). The tin–proton coupling constants are given as the average of the ^{117}Sn and ^{119}Sn values. For compounds containing the Me_3Sn group, high-resolution molecular mass measurements were determined on the $M^+ - Me$ fragment[11] and are based on ^{120}Sn. GLC analyses were performed with a Hewlett-Packard Model 5890 gas chromatograph equipped with a 25 m × 0.21 mm fused silica column coated with cross-linked SE-54. TLC analyses were carried out with commercial aluminum-backed silica gel plates (E. Merck, type 5554). Column chromatography and flash chromatography[8] were done with 70–230 and 230–400 mesh silica gel (E. Merck), respectively. All purified products exhibited one spot on TLC analysis and/or essentially one peak on GLC analysis.

(8) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(9) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.
(10) Intermediates derived from the reaction of α,β-acetylenic esters with alkylcuprate reagents may be trapped with electrophiles. Examples may be found in Taylor, R. J. K. *Synthesis* **1985**, 364.
(11) Kuivila, H. G.; Tsai, K.-H.; Kingston, D. G. I. *J. Organomet. Chem.* **1970**, *23*, 129.

Preparation of $Me_3SnCu(2\text{-Th})(CN)Li_2$ (10).[6] To a cold (−20 °C), stirred solution of $(Me_3Sn)_2$ (164 mg, 0.5 mmol) in 10 mL of dry THF were added, successively, thiophene (42 mg, 0.5 mmol) and a solution of MeLi (1.0 mmol, low halide or LiBr complex) in Et_2O. After the pale yellow solution had been stirred at −20 °C for 50 min, it was cooled to −78 °C and CuCN (45 mg, 0.5 mmol) was added. The resulting suspension was stirred for 5 min at −78 °C and for 10 min at −48 °C to provide a bright yellow solution of the cuprate reagent **10**. The solution was cooled to −78 °C and used immediately.

3-Methyl-3-(trimethylstannyl)cyclohexanone (18). To a cold (−78 °C), stirred solution of reagent **10** (0.5 mmol) in 10 mL of dry THF (argon atmosphere) was added 37 mg (0.33 mmol) of the enone **11**. After the solution had been stirred at −78 °C for 5 min and at −20 °C for 4 h, it was treated with saturated aqueous NH_4Cl–NH_4OH (pH 8) (10 mL) and Et_2O (10 mL). The vigorously stirred mixture was exposed to air and allowed to warm to room temperature. The phases were separated, and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Flash chromatography[8] (1:4 Et_2O–petroleum ether) of the residual oil, followed by distillation (90 °C/2.0 Torr) of the material thus obtained, gave 83 mg (90%) of compound **18**: IR (neat) 1713, 1452, 1224, 768 cm^{-1}; ^1H NMR (300 MHz) δ 0.06 (s, 9 H, $^2J_{Sn-H}$ = 50 Hz), 1.20 (s, 3 H, $^3J_{Sn-H}$ = 60 Hz), 1.55–2.60 (series of m, 10 H); exact mass calcd for $C_9H_{17}OSn$ (M^+ − Me) 261.0301, found 261.0306.

3,5,5-Trimethyl-3-(trimethylstannyl)cyclohexanone (19). Via a procedure identical with that described above, 46 mg (0.33 mmol) of the enone **12** was converted into 88 mg (87%) of compound **19** (distillation temperature 90 °C/2.0 Torr), a colorless oil that was spectrally identical with the same substance prepared previously.[1b]

Preparation of Compounds 20 and 21. Reaction of the enone **13** (51 mg, 0.33 mmol) with reagent **10** was carried out as described above, except that the reaction time was 2 h rather than 4 h. Analysis of the crude product by GLC showed that the epimers **20** and **21** were present in a ratio of 3:1, respectively. Flash chromatography[8] (3:97 Et_2O–petroleum ether) of the mixture, followed by distillation (90–100 °C/2.0 Torr) of the two oils thus obtained, gave 74 mg (69%) of **20** and 21 mg (20%) of **21**. Trans isomer **20**: IR (neat) 1705, 1457, 764 cm^{-1}; ^1H NMR (300 MHz) δ 0.00 (s, 9 H, $^2J_{Sn-H}$ = 48 Hz), 1.00 (d, 3 H, J = 6 Hz), 1.03, 1.07 (s, s, 3 H each, $^3J_{Sn-H}$ = 65 Hz in each case), 1.32 (br t, 2 H), 1.70–2.05 (m, 3 H), 2.15 (m, 2 H), 2.30 (m, 1 H); exact mass calcd for $C_{12}H_{23}OSn$ (M^+ − Me) 303.0771, found 303.0763.

Cis isomer **21**: IR (neat) 1704, 1467, 763 cm^{-1}; ^1H NMR (300 MHz) δ 0.00 (s, 9 H, $^2J_{Sn-H}$ = 49 Hz), 0.90 (d, 3 H, J = 9 Hz), 1.03, 1.06 (s, s, 3 H each, $^3J_{Sn-H}$ = 65 Hz in each case), 1.56–1.65 (m, 2 H), 1.82–2.23 (m, 4 H), 2.40–2.55 (m, 2 H); exact mass calcd for $C_{12}H_{23}OSn$ (M^+ − Me) 303.0771, found 303.0765. When pure **21** was treated with MeONa in MeOH (room temperature, overnight), an 88:12 mixture of **20** and **21**, respectively, was produced.

Preparation of the Ester 22. Reaction of the α,β-unsaturated ester **14** (42 mg, 0.33 mmol) with reagent **10** was carried out at −78 °C for 1 h and at −20 °C for 30 min, by using a procedure similar to that described above. Flash chromatography (3:97 Et_2O–petroleum ether) of the crude product, followed by distillation (120 °C/2.0 Torr) of the oil thus obtained, gave 76 mg (91%) of the ester **22**: IR (neat) 1729, 1186, 1163, 766 cm^{-1}; ^1H NMR (300 MHz) δ 0.04 (s, 9 H, $^2J_{Sn-H}$ = 49 Hz), 1.22 (t, 3 H, J = 8 Hz), 1.3 (m, 5 H), 1.6 (m, 3 H), 1.85 (m, 2 H), 2.45 (s, 2 H, $^3J_{Sn-H}$ = 72 Hz), 4.07 (q, 2 H, J = 8 Hz); exact mass calcd for $C_{12}H_{23}O_2Sn$ (M^+ − Me) 319.0720, found 319.0718.

3-(Trimethylstannyl)hexanal (23), (*Z*)-3-(Trimethylstannyl)-6-nonenal (24), and the Aldehyde 25. These substances were prepared from the α,β-unsaturated aldehydes **15**[12] (33 mg, 0.33 mmol), **16**[12] (46 mg, 0.33 mmol), and **17**[13] (41 mg, 0.33 mmol), respectively, via a procedure similar to that described above. In each case, the reaction was carried out at −78 °C for 1 h and at −20 °C for 1 h. Flash chromatography[8] (1:4 Et_2O–petroleum ether) of the crude products, followed by distillation (**23**, 50 °C (2.0 Torr); **24**, 75–80 °C (2.0 Torr); **25**, 120 °C (2.0 Torr)) of the oils thus obtained, afforded 54 mg (61%) of **23**, 65 mg (64%) of **24**, and 60 mg (62%) of **25**.

Compound **23**: IR (neat) 2718, 1723, 1186, 764 cm^{-1}; ^1H NMR (300 MHz) δ 0.04 (s, 9 H, $^2J_{Sn-H}$ = 51 Hz), 0.87 (t, 3 H, J = 8 Hz), 1.38–1.70 (m, 5 H), 2.65 (dd, 2 H, J = 4, 1.5 Hz), 9.74 (t, 1 H, J = 1.5 Hz); exact mass calcd for $C_8H_{17}OSn$ (M^+ − Me) 249.0301, found 249.0304.

Compound **24**: IR (neat) 2715, 1724, 1187, 767 cm^{-1}; ^1H NMR (300 MHz) δ 0.05 (s, 9 H, $^2J_{Sn-H}$ = 50 Hz), 0.93 (t, 3 H, J = 7 Hz), 1.4–1.75 (m, 3 H), 1.85–2.15 (m, 4 H), 2.68 (dd, 2 H, J = 6.5, 1.3 Hz), 5.33 (m, 2 H), 9.75 (t, 1 H, J = 1.3 Hz); exact mass calcd for $C_{11}H_{21}OSn$ (M^+ − Me) 289.0614, found 289.0617.

Compound **25**: IR (neat) 2722, 1720, 1450, 896, 767 cm^{-1}; ^1H NMR (300 MHz) δ 0.05 (s, 9 H, $^2J_{Sn-H}$ = 49 Hz), 1.15–1.44 (m, 5 H), 1.76–2.04 (m, 2 H), 2.60 (d, 2 H, J = 1.6 Hz, $^3J_{Sn-H}$ = 67 Hz), 9.77 (t, 1 H, J = 1.6 Hz); exact mass calcd for $C_{10}H_{19}OSn$ (M^+ − Me) 275.0458, found 275.0457.

Ethyl 4-(Methoxymethoxy)-2-butynoate (26). To a stirred solution of 2-propyn-1-ol (3 g, 53.5 mmol) in 100 mL of dry CH_2Cl_2 (argon atmosphere) was added *N,N*-diisopropylethylamine (18.6 mL, 107 mmol), and the mixture was cooled to 0 °C. Chloromethyl methyl ether (7.7 mL, 101.7 mmol) was added dropwise, and the mixture was stirred overnight. Saturated aqueous $NaHCO_3$ (50 mL) was added, and the two phases were separated. The organic phase was washed with 5% hydrochloric acid (2 × 10 mL) and brine (2 × 10 mL), dried ($MgSO_4$), and concentrated. Distillation (~115 °C/atmospheric pressure) of the remaining oil gave 4.43 g (83%) of 3-(methoxymethoxy)-1-propyne.

To a cold (−78 °C), stirred solution of 2.5 g (0.25 mmol) of 3-(methoxymethoxy)-1-propyne in 100 mL of dry THF was added a solution of MeLi (0.27 mmol) in Et_2O, and the mixture was stirred at −78 °C for 10 min and at −20 °C for 1 h. EtO_2CCl (4.78 mL, 50 mmol) was added, and the mixture was stirred at −20 °C for 40 min and at room temperature for 2 h. Saturated aqueous $NaHCO_3$ (30 mL) and Et_2O (50 mL) were added, and the phases were separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (2 × 10 mL), dried ($MgSO_4$), and concentrated. Distillation (90 °C/2.0 Torr) of the remaining oil gave 3.15 g (73%) of the α,β-acetylenic ester **26**: IR (neat) 2239, 1713, 1368, 1153 cm^{-1}; ^1H NMR (400 MHz) δ 1.32 (t, 3 H, J = 8 Hz), 3.40 (s, 3 H), 4.24 (q, 2 H, J = 8 Hz), 4.35 (s, 2 H), 4.72 (s, 2 H); exact mass calcd for $C_8H_{12}O_4$ 172.0736, found 172.0699.

Reaction of Reagent 10 with 5. To a cold (−78 °C), stirred solution of the cuprate **10** (0.5 mmol) in 10 mL of dry THF (argon atmosphere) was added a solution of 93 mg (0.38 mmol) of the α,β-acetylenic ester **5**[2b,c] in 0.5 mL of dry THF. The mixture was stirred at −78 °C for 2 h. Workup was carried out as described previously (preparation of **18**). Analysis (GLC) of the crude product showed that it consisted of a 95:5 mixture of **27** and **29**, respectively. Flash chromatography[8] (3:97 Et_2O–petroleum ether) of the mixture, followed by distillation (110 °C/2.0 Torr) of the oil thus obtained, provided 102 mg (65%) of pure **27**, which exhibited spectra identical with those of the same substance reported previously.[2b,c]

Reaction of Reagent 10 with 26. A procedure identical with that described above was employed. The crude product obtained from 65 mg (0.38 mmol) of the α,β-acetylenic ester **26** consisted (GLC analysis) of a 9:1 mixture of **28** and **30**, respectively. Flash chromatography[8] (3:97 Et_2O–petroleum ether) of this mixture, followed by distillation (~130 °C/2.0 Torr) of the oil thus obtained, gave 72 mg (55%) of pure **28**: IR (neat) 1703, 1608, 1198, 1040, 775 cm^{-1}; ^1H NMR (300 MHz) δ 0.2 (s, 9 H, $^2J_{Sn-H}$ = 56 Hz), 1.29 (t, 3 H, J = 8 Hz), 3.40 (s, 3 H), 4.22 (q, 2 H, J = 8 Hz), 4.39 (d, 2 H, J = 3 Hz, $^3J_{Sn-H}$ = 30 Hz), 4.69 (s, 2 H), 6.69 (t, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 108 Hz); exact mass calcd for $C_{10}H_{19}O_4Sn$ (M^+ − Me) 323.0305, found 323.0298.

Ethyl (*Z*)-4-(*tert*-Butyldimethylsiloxy)-2-methyl-3-(trimethylstannyl)-2-butenoate (31). To a cold (−78 °C), stirred solution of the cuprate **10** (0.5 mmol) in 10 mL of dry THF (argon atmosphere) was added slowly a solution of the α,β-acetylenic ester **5** (81 mg, 0.33 mmol) in 0.5 mL of dry THF. After the mixture had been stirred at −78 °C for 1 h and at −20 °C for 30 min, HMPA (3.3 mmol) and MeI (8 mmol) were added successively. The solution was stirred at −20 °C for 30 min and at room temperature for 1 h. Saturated aqueous NH_4Cl–NH_4OH (pH 8) (10 mL) and

(12) This substance is commercially available.
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Et_2O (10 mL) were added, and the vigorously stirred mixture was exposed to air until the aqueous phase was deep blue (~15 min). The phases were separated, and the aqueous phase was extracted with Et_2O (4 × 10 mL). The combined organic extracts were washed with saturated aqueous $CuSO_4$ (3 × 10 mL) and brine (2 × 10 mL) and then were dried ($MgSO_4$) and concentrated. Flash chromatography[8] (3:97 Et_2O–petroleum ether) of the crude product and distillation (~130 °C/2.0 Torr) of the oil thus obtained gave 91 mg (65%) of the ester **31**: IR (neat) 1702, 1599, 1176, 1274, 838, 776 cm^{-1}; ^1H NMR (300 MHz) δ 0.04 (s, 6 H), 0.11 (s, 9 H, $^2J_{Sn-H}$ = 55 Hz), 0.87 (s, 9 H), 1.28 (t, 3 H, J = 7 Hz), 1.93 (s, 3 H, $^4J_{Sn-H}$ = 7.1 Hz), 4.17 (q, 2 H, J = 7 Hz), 4.40 (s, 2 H, $^3J_{Sn-H}$ = 48 Hz); exact mass calcd for $C_{15}H_{31}O_3SiSn$ (M^+ – Me) 407.1072, found 407.1064.

Ethyl (*Z*)-4-(*tert*-Butyldimethylsiloxy)-2-(2-propenyl)-3-(trimethylstannyl)-2-butenoate (32). This material was prepared via a procedure very similar to that described above, except that 5.5 mmol of alkylating agent (3-iodopropene) was used and the reaction was carried out at –20 °C for 30 min. Distillation (115 °C/2.0 Torr) of the final product gave 91 mg (60%) of pure **32**: IR (neat) 3080, 1703, 1639, 1154, 1073, 776 cm^{-1}; ^1H NMR (300 MHz) δ 0.03 (s, 6 H), 0.13 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 0.86 (s, 9 H), 1.26 (t, 3 H, J = 8 Hz), 3.14 (m, 2 H), 4.16 (q, 2 H, J = 8 Hz), 4.39 (s, 2 H, $^3J_{Sn-H}$ = 49 Hz), 4.93 (m, 1 H), 4.98 (m, 1 H), 4.77 (m, 1 H); exact mass calcd for $C_{17}H_{33}O_3SiSn$ (M^+ – Me) 433.1221, found 433.1216.

Ethyl (*Z*)-4-(*tert*-Butyldimethylsiloxy)-2-(2-propynyl)-3-(trimethylstannyl)-2-butenoate (33). A procedure similar to that outlined above was employed, except that 1.67 mmol of alkylating agent (3-bromopropyne) was used and the reaction was carried out at –78 °C for 1 h and at –20 °C for 1 h. The crude product consisted of a 3:1 mixture of **33** and the corresponding protonation products **27** and **29**. Distillation (140 °C/2.0 Torr) of the appropriate oil derived from chromatography afforded 59 mg (40%) of pure **33**: IR (neat) 3312, 2121, 1704, 1599, 1206, 1043, 839, 779 cm^{-1}; ^1H NMR (300 MHz) δ 0.06 (s, 6 H), 0.15 (s, 9 H, $^2J_{Sn-H}$ = 56 Hz), 0.87 (s, 9 H), 1.30 (t, 3 H, J = 7 Hz), 1.94 (t, 1 H, J = 2.8 Hz), 3.31 (d, 2 H, J = 2.8 Hz), 4.22 (q, 2 H, J = 7 Hz), 4.49 (s, 2 H, $^3J_{Sn-H}$ = 44 Hz); exact mass calcd for $C_{17}H_{31}O_3SiSn$ (M^+ – Me) 431.1064, found 431.1059.

Ethyl 6-Iodo-2-hexynoate (35). To a cold (–78 °C) stirred solution of 5-chloro-1-pentyne (2 g, 19.5 mmol) in 100 mL of dry THF (argon atmosphere) was added a solution of MeLi (19.5 mmol) in Et_2O. After the mixture had been stirred at –78 °C for 10 min and at –20 °C for 45 min, EtO_2CCl (2.8 mL, 29 mmol) was added, and stirring was continued at –20 °C for 1 h and at room temperature for 1 h. Saturated aqueous $NaHCO_3$ (30 mL) and Et_2O (50 mL) were added, and the phases were separated. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Distillation (85–90 °C/2.0 Torr) of the residual oil gave 3.0 g (88%) of ethyl 6-chloro-2-hexynoate (**34**).

To a soluton of NaI (17.2 g, 115 mmol) in dry acetone (150 mL) (argon atmosphere) was added a solution of the chloro ester **34** (2 g, 11.5 mmol) in 10 mL of dry acetone, and the mixture was refluxed overnight. Most of the solvent was removed, and water (50 mL) and Et_2O (50 mL) were added to the residue. The phases were separated, and the aqueous phase was washed with Et_2O (2 × 20 mL). The combined extracts were dried ($MgSO_4$) and concentrated. Distillation (100–110 °C/2.0 Torr) of the remaining oil gave 2.62 g (86%) of the iodo ester **35**: IR (neat) 2237, 1703, 1273, 1078 cm^{-1}; ^1H NMR (300 MHz) δ 1.26 (t, 3 H, J = 8 Hz), 2.02 (m, 2 H), 2.45 (t, 2 H, J = 8 Hz), 3.24 (t, 2 H, J = 8 Hz), 4.17 (q, 2 H, J = 8 Hz); exact mass calcd for $C_8H_{11}IO_2$ 265.9804, found 265.9815.

Ethyl 2-(Trimethylstannyl)-1-cyclopentenecarboxylate (36). To a cold (–78 °C), stirred solution of the cuprate reagent **10** (0.5 mmol) in 10 mL of dry THF (argon atmosphere) was added a solution of the iodo ester **35** (102 mg, 0.38 mmol) in 0.5 mL of dry THF, and the mixture was stirred at –78 °C for 2 h and at –48 °C for 1 h. The workup procedure was identical with that described previously (see preparation of **18**). Flash chromatography (3:97 Et_2O–petroleum ether) of the crude product and distillation (110 °C/2.0 Torr) of the oil thus obtained produced 73 mg (62%) of the pure ester **36**: IR (film) 1699, 1592, 1187, 768 cm^{-1}; ^1H NMR (400 MHz) δ 0.17 (s, 9 H, $^2J_{Sn-H}$ = 50 Hz), 1.27 (t, 3 H, J = 6 Hz), 1.90 (m, 2 H), 2.49 (br t, 4 H), 4.18 (q, 2 H, J = 6 Hz); exact mass calcd for $C_{10}H_{17}O_2Sn$ (M^+ – Me) 289.0250, found 289.0252.

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Generation and Cycloaddition Reactions of Phenylthio Nitrile Oxide. A Preparation of 3-(Phenylthio)- and 3-(Phenylsulfonyl)-Δ^2-isoxazolines

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The research of Wade and co-workers[2] has established that 3-(phenylsulfonyl)-Δ^2-isoxazolines are versatile synthetic intermediates (Scheme I). These isoxazolines are usually prepared by 1,3-dipolar cycloaddition reactions of phenylsulfonyl nitrile oxide. For example, the treatment of oxime bromide **1** with aqueous sodium carbonate in the presence of an alkene gives 3-(phenylsulfonyl)-Δ^2-isoxazolines **2**.[2c] The phenylsulfonyl group of **2** can be displaced by a variety of nucleophiles[2c] to provide substituted isoxazolines **3**, some of which are not directly available by nitrile oxide cycloaddition reactions. Subsequent hydrogenolytic cleavage of **3** gives β-hydroxy ketones or esters **4**.[3] β-Hydroxy nitriles are directly available by reduction of **2** with 2% sodium amalgam.[2e]

Oxime bromide **1** is an excellent precursor for small-scale preparations of **2**. However, practical problems arise on a preparative scale: several steps are needed to prepare **1** from phenylsulfonylnitromethane, a relatively low overall yield is obtained, and a large quantity of diazomethane is required at one stage. The cycloaddition procedure often uses a large excess of olefin, perhaps due to the tendency of the highly reactive phenylsulfonyl nitrile oxide to dimerize. To circumvent these problems, other useful methods to generate phenylsulfonyl nitrile oxide have been developed.[2,4] We now report a practical, two-step method for the preparation of 3-(phenylsulfonyl)-Δ^2-isoxazolines **2**. Phenylthioisoxazolines **6**[5] are readily available from dipolar cycloaddition reactions of phenylthio nitrile oxide with alkenes, and they are rapidly oxidized to 3-(phenylsulfonyl)-Δ^2-isoxazolines by *m*-chloroperoxybenzoic acid.

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