mixture of starting material and monobenzylidine and dibenzylidine derivatives. An alternative four-step sequence employing Boekelheide rearrangement of an acetylated *N*-oxide[11] proved more convenient (Figure 1). Thus, the *N*-oxide of **6** was treated with hot, deoxygenated acetic anhydride, hydrolyzing the resulting acetate in situ to afford **7**.[8] Oxidation of this alcohol with chromic acid in aqueous acetic acid[12] gave ketone **8**[8] in 63% yield overall from **6**.

Conversion of **8** to hepatcyclic terpyridine **3** requires symmetrical coupling of a ketone with the introduction of a carbon at C-4 of the new pyridine ring. Thummel used the reaction of an enamine with formaldehyde, followed by aromatization of the resulting diketone, to prepare a tetrahydro derivative of **1**.[4] Newkome and Fishel have reported an unusual pyridine synthesis, in which C-4 is introduced by methyl migration in the pyrolysis of trimethylhydrazonium salts of aromatic ketones.[13] We have found that this remarkable reaction may be applied to hexahydro-4-acridinones (Figure 1). Thus, **8** is converted first to the dimethylhydrazone and then to the trimethylhydrazonium salt **9** by alkylation with trimethyloxonium tetrafluoroborate. Pyrolysis of the crude salt at 210 °C under a stream of nitrogen, followed by recrystallization from ethanol, gave the heptacyclic terpyridine **3**[14] in 23% yield overall from **8**. The product was obtained as the sesquihydrate in the form of straw-colored needles (mp 220–221 °C), which were soluble in many organic solvents (e.g., CH_2Cl_2, $CHCl_3$, pyridine, 2-propanol, DMF, and acetic acid) and slightly soluble in others (e.g., benzene, acetonitrile, ether, THF, and ethanol).

Heptacyclic terpyridine **3** differs from **2** in the presence of flexible substituents and saturated terminal rings. These features make **3** particularly suitable as a precursor to hexaazakekulene derivatives, such as **4**. Oxidative functionalization of **3** and methods for pyridine synthesis by unsymmetrical coupling of two ketones are currently under investigation.

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Registry No. **3**, 99922-89-1; **5**, 24133-22-0; **6**, 99922-90-4; **7**, 99922-91-5; **8**, 99922-92-6; **9**, 99922-94-8; $NH_2OH{\cdot}HCl$, 5470-11-1; Me_2NNH_2, 57-14-7; cyclohexanone, 108-94-1; valeraldehyde, 110-62-3.

(11) Review: Traynelis, V. J. In "Mechanisms of Molecular Migrations"; Thyagarajan, B. S., Ed.; Interscience: New York, 1969; Vol. 2, pp 1–42. See also: Cohen, T.; Deets, G. L. *J. Am. Chem. Soc.* **1972**, *94*, 932–938.

(12) Yanagida, A. J.; Gansser, C. *J. Heterocycl. Chem.* **1978**, *15*, 249–251.

(13) Newkome, G. R.; Fishel, D. L. *J. Org. Chem.* **1972**, *37*, 1329–1336.

(14) ^1H NMR (80 MHz, $CDCl_3$, δ relative to Me_4Si) 7.36 (s, 1 H, Ar H), 3.8 (br s, 3 H, H_2O), 3.0–3.2 (m, 4 H, α-$PyCH_2$), 2.92 (s, 8 H, $ArCH_2CH_2Ar$), 2.5–2.9 (m, 8 H, Ar CH_2), 1.7–1.9 (m, 8 H, $CH_2CH_2CH_2CH_2$), 1.25–1.5 (m, 8 H, $CH_2CH_2CH_2CH_3$), 0.97 (t, 6 H, CH_3); IR (KBr) 3350 (br), 2940 (s), 2850 (ms), 1650 (sh), 1550 (m), 1430 (m), 1390 (m), 1240 (m), cm^{-1}; UV (95% EtOH) λ_{max} (ϵ) 245 (22 000), 297 (10 000), 306 (14 000), 346 (24 000), nm; MS (70 eV), *m/e* (relative intensity) 505 (M^+, 100). Anal. Calcd for $C_{35}H_{46}N_3O_{1.5}$: C, 78.90; H. 8.70; N, 7.89. Found: C, 78.73; H, 8.68; N, 7.65.

(15) **Note added in proof**: An alternate approach to unsubstituted hexaazakekulene derivatives has appeared recently: Ransohoff, J. E. B.; Staab, H. A. *Tetrahedron Lett.* **1985**, *26*, 6179–6182.

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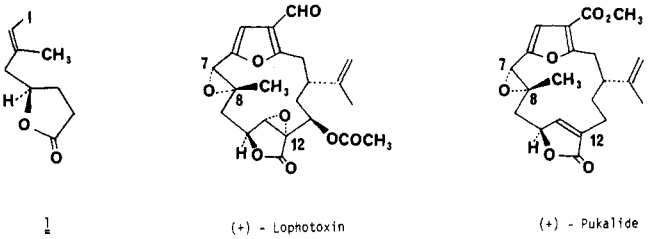
Synthesis of a Lophotoxin Intermediate

Summary: The carbometalation of an optically active homopropargyl alcohol is the key step in preparing the C-7,C-12 fragment of the marine neuromuscular agent (+)-lophotoxin.

Sir: During the course of our synthetic study of the related marine furanocembranoids (+)-lophotoxin[1] and (+)-pukalide,[2] we wished to prepare lactone **1**. The vinyl iodide



1 (+) - Lophotoxin (+) - Pukalide

provides the functionality that is needed to form the C-6,C-7 bond of the natural products either through palladium(0)[3] or rhodium(I)-catalyzed[4] coupling to a furyl nucleophile. Control of the geometry of the trisubstituted alkene is crucial to the success of this approach. The zirconocene dichloride mediated addition of trimethylaluminum to an alkyne[5] appeared to offer a convenient solution to this problem. This reaction has been reported to be successful with unprotected homopropargyl alcohols;[5] therefore the reaction with racemic alcohol **2** was examined (Scheme I). The preparation of **2** from 1,4-butanediol was straightforward; however, the yield of the following synthetic step, carbometalation[5] followed by quenching with iodine, was disappointing (35% isolated yield of **3a**). Silyl ether **4** was prepared and was subjected to the same reaction conditions. The yield was again unacceptably low (20% isolated yield of **3b**). In neither reaction was there any evidence of unreacted starting material.

The conceptual simplicity of the carbometalation–iodination[5] sequence suggested that this approach to the C-7,C-12 fragment be pursued. Since homopropargyl alcohols have been shown to be good substrates for this reaction it was reasonable to assume that the remote oxygen was responsible for the poor yields of **3a** and **3b**. Accordingly 7-(phenylthio)hept-1-yn-4-ol (**5**) and 7-chlorohept-1-yn-4-ol (**6**) were prepared (Scheme II). Carbometalation[5] of **5** and **6** followed by iodination produced vinyl iodides **7** (70–80% yield) and **8** (76–82% yield), respectively. The vastly improved yields for the reactions of **5** and **6** suggested that the earlier results with **2** and **4** were a consequence of bidentate chelation of aluminum by both oxygen atoms.

The introduction of the second oxygen atom could be accomplished either through a Pummerer[10] reaction of **7**

(1) Fenical, W.; Okuda, R. K.; Bandurraga, M. M.; Culver, P.; Jacobs, R. S. *Science (Washington, D.C.)* **1981**, *212*, 1512–1514.

(2) Missakian, M. G.; Burreson, B. J.; Scheuer, P. J. *Tetrahedron* **1975**, *31*, 2513–2515.

(3) Negishi, E.-i.; Luo, F.-T.; Frisbee, R.; Matsushita, H. *Heterocycles* **1982**, *18*, 117–122.

(4) Larock, R. C.; Narayanan, K.; Hershberger, S. S. *J. Org. Chem.* **1983**, *48*, 4377–4380.

(5) (a) Rand, C. L.; Horn, D. E. V.; Moore, M. W.; Negishi, E. *J. Org. Chem.* **1981**, *46*, 4093–4096. (b) For a review, see: Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333–2356.

(6) Lombardo, L. *Tetrahedron Lett.* **1984**, 227–228.

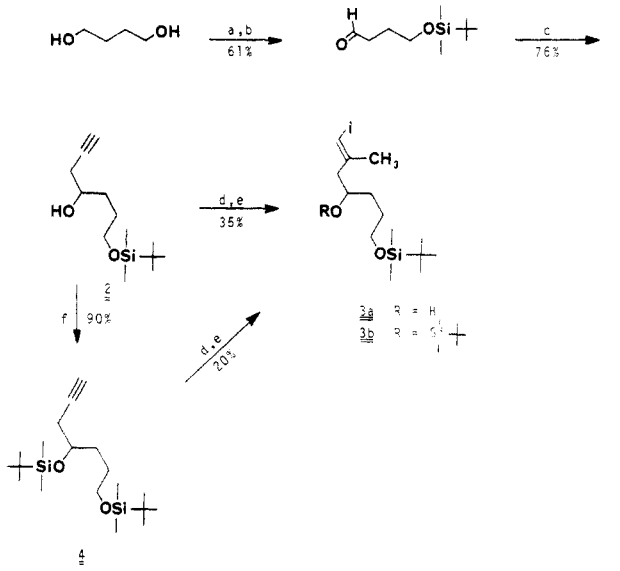
(7) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650.

(8) Propargylmagnesium bromide was prepared from propargyl bromide and magnesium in the presence of catalytic mercuric chloride: Sondheimer, F.; Amiel, Y.; Gaoni, Y. *J. Am. Chem. Soc.* **1962**, *84*, 270–274.

(9) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.

0022-3263/86/1951-0765$01.50/0

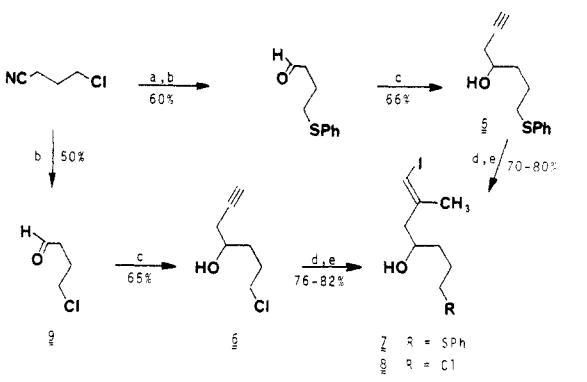
Scheme I[a]



[a] (a) *t*-BuMe$_2$SiCl (0.4 equiv), *i*-Pr$_2$NEt (0.6 equiv), CH_2Cl_2, 25 °C, 12 h;[6] (b) PCC, NaOAc, CH_2Cl_2, 25 °C; (c) HC≡CCH$_2$MgBr, Et_2O, −30 to 25 °C;[8] (d) Me_3Al (3.0 equiv), $ZrCp_2Cl_2$ (1.0 equiv), CH_2Cl_2, 45 °C;[5] (e) I_2 (1.2 equiv), THF;[5] (f) *t*-BuMe$_2$SiCl (1.1 equiv), imidazole (1.5 equiv), DMF, 25 °C.[9]

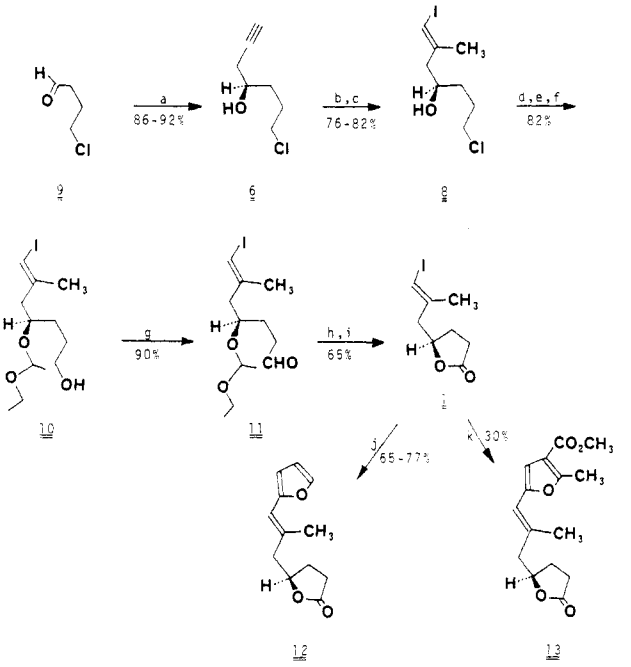
or by nucleophilic displacement of chloride **8** by acetate ion. The acetate displacement reaction was found to be most convenient and was used for the enantioselective preparation of **1**. (+)-Diisopropyl tartrate mediated addition of allenylboronic acid[11] to aldehyde **9** furnished homopropargyl alcohol (*R*)-**6**[12a] (43% ee,[13] unoptimized, $[\alpha]^{21}_D$ +10.3° (*c* 3.60, CH_2Cl_2) in 86–92% isolated yield (Scheme III). Carbometalation[5] of **6** with 3 equiv of trimethylaluminum and 0.25 equiv of zirconocene dichloride at 50 °C followed by cooling to −30 °C and treatment with 1.2 equiv of iodine upon gradual warming to 0 °C furnished (*R*)-**8**[12b] in 76–82% isolated yield. Protection[14] of the secondary alcohol in **8** was necessary to

Scheme II[a]



[a] (a) PhSH, Et_3N, DMF, 25 °C; (b) DIBAL, CH_2Cl_2, −78 to 25 °C; (c) HC≡CCH$_2$MgBr, Et_2O, −30 to 25 °C;[8] (d) Me_3Al (3.0 equiv), $ZrCp_2Cl_2$ (1.0 equiv), $ClCH_2CH_2Cl$, 50 °C;[5] (e) I_2 (1.2 equiv), THF, −30 to 0 °C.[5]

Scheme III[a]



[a] (a) CH_2=C=CHB(OH)$_2$, (+)-DIPT, toluene, −78 °C, 40 h;[11] (b) Me_3Al (3.0 equiv), $ZrCp_2Cl_2$ (0.25 equiv), $ClCH_2CH_2Cl$, 50 °C;[5] (c) I_2 (1.2 equiv), THF, −30 to 0 °C; (d) CH_2=CHOCH$_2$CH$_3$, PPTS, CH_2Cl_2, 25 °C;[14] (e) KOAc, DMF, 18-crown-6, 100 °C; (f) K_2CO_3, CH_3OH, 25 °C; (g) Me_2SO, ClCOCOCl, THF, Et_3N, −78 to 0 °C;[15] (h) PPTS, THF–H_2O (5:1), 25 °C;[14] (i) PCC, CH_2Cl_2, 25 °C;[7] (j) furylzinc chloride, $(PPh_3)_2PdCl_2$ (0.07 equiv), DIBAL (0.15 equiv), THF, 25 °C;[3] (k) methyl-5-(chloromercuric)-2-methyl-3-furancarboxylate, 10 mol % $RhCl(PPh_3)_3$, LiCl (10.0 equiv), HMPA, 70 °C.[4]

prevent competitive cyclization to a furan during the displacement of chloride by acetate. Acetate hydrolysis was followed by a Swern oxidation[15] of the primary alcohol to produce aldehyde **11**. Hydrolysis[14] of the ethoxyethyl protecting group and oxidation of the lactol with pyridinium chlorochromate[7] furnished lactone **1**,[12c] $[\alpha]^{21}_D$ −25.1° (*c* 1.43, CH_2Cl_2). The palladium(0)-catalyzed[3] addition of furylzinc chloride[12d] to **1** took place in 65–77% isolated yield. A more densely functionalized furyl lactone was prepared from methyl 2-methyl-3-furancarboxylate. Mercuration[16] with mercuric chloride and sodium acetate

(10) (a) Iriuchijima, S.; Maniwa, K.; Tsuchihashi, G.-i. *J. Am. Chem. Soc.* **1974**, *96*, 4280–4283. (b) Ikeda, T.; Hutchinson, C. R. *J. Org. Chem.* **1984**, *49*, 2837–2838.

(11) Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667–7669.

(12) (a) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.81 (m, 1 H), 3.60 (m, 2 H), 2.40 (m, 2 H), 2.09 (t, *J* = 2.5 Hz, 1 H), 2.05–1.60 (complex m, 4 H); IR (neat) 3414, 3300, 2924, 2119, 1444, 1307 cm^{-1}. (b) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.01 (s, 1 H), 3.75 (m, 1 H), 3.56 (m, 2 H), 2.37 (m, 2 H), 2.05–1.45 (complex m, 2 H), 1.86 (s, 3 H); IR (neat) 3368, 2930, 1668, 1616, 1444, 1373, 1273, 1142 cm^{-1}; mass spectrum, *m/e* 290 (M^+ + 2), 288 (M^+), 273 271, 211, 183, 182, 181, 167, 163, 161, 128, 127, 109, 108, 107, 105, 43 (100%). (c) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.10 (s, 1 H), 4.66 (m, 1 H), 2.56 (m, 3 H), 2.32 (m, 1 H), 1.90 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.52, 142.63, 78.47, 78.21, 44.68, 28.41, 27.47, 24.23; IR (neat) 2949, 1776, 1618, 1456, 1417, 1377, 1352, 1280, 1180 cm^{-1}; mass spectrum, *m/e* 267 (M^+ + 1), 266 (M^+), 181, 141, 140, 139, 128, 127, 95, 93, 87, 86, 85 (100%), calcd for $C_8H_{11}IO_2$ 265.978, found 265.980. (d) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 1.5 Hz, 1 H), 6.39 (dd, *J* = 3.2, 1.7 Hz, 1 H), 6.23 (d, *J* = 3.2 Hz, 1 H), 6.16 (s, 1 H), 4.69 (m, 1 H), 2.65 (m, 3 H), 2.35 (m, 2 H), 2.10 (s, 3 H), 1.95 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.78, 152.61 140.88, 132.04, 117.17, 110.92, 108.39, 79.11, 46.09, 28.49, 27.46, 18.84; IR (neat) 2943, 1776, 1658, 1491, 1460, 1421, 1381, 1356, 1288, 1265, 1215, 1180 cm^{-1}; mass spectrum, *m/e* 207 (M^+ + 1), 206 (M^+), 133, 122, 121 (100%), 93, 91, 85. (e) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.40 (s, 1 H), 6.02 (s, 1 H), 4.63 (m, 1 H), 3.78 (s, 3 H), 2.52 (s, 3 H), 2.61–2.2 (m, 3 H), 1.96 (s, 3 H), 1.90 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.83, 164.45, 157.74, 150.47, 133.39, 116.62, 114.49, 108.79, 79.09, 51.33, 46.22, 28.62, 27.65, 19.09, 13.78; IR (neat) 2953, 1776, 1718, 1604, 1556, 1444, 1410, 1371, 1354, 1278, 1238, 1180, 1143, 1091, 1047, 1010; mass spectrum, *m/e* 279 (M^+ + 1), 278 (M^+), 247, 246, 194, 193, 162, 161, 128, 119, 91, 85 (100%).

(13) Enantiomeric excess was determined by Mosher analysis: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

(14) Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772–3774.

(15) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482.

in water–ethanol (10:1) followed by rhodium(I)-catalyzed[4] coupling to 1 produced 13[12e] in modest yield (30%). The stereochemical integrity of the trisubstituted double bond in the both 12 and 13 is preserved, as evidenced by the ^{13}C NMR spectrum.[12d,12e]

In summary, an enantioselective synthesis of a lophotoxin intermediate has been described. The problems of conducting the carbometalation reaction on oxygenated substrates have been identified, and a general solution has been developed. Work in progress has indicated that substituted furyl nucleophiles undergo rhodium(I)-catalyzed coupling to 1 without interference by the carboxylate on the furan or by the lactone carbonyl group.[17]

Acknowledgment is made to the National Science Foundation (CHE-84-03495) for support of this work. NSF Grant CHE-81-00240 supported the purchase of the 300-MHz NMR spectrometer.

Supplementary Material Available: Experimental details for the coupling reactions leading to 12 and 13 (1 page). Ordering information is given on any current masthead page.

(16) Gilman, H.; Burtner, R. R. *J. Am. Chem. Soc.* **1949**, *71*, 1213–1215.

(17) A reviewer suggested that the cross-coupling might be performed directly on the vinylzirconium intermediate and a furyl halide. This approach was examined in a model study. 4-[(*tert*-Butyldimethylsilyl)oxy]-dec-1-yne was subjected to the carbometalation reaction followed by Pd(0)- or Ni(0)-catalyzed coupling with iodo- or bromobenzene to give 4-[(*tert*-butyldimethylsilyl)oxy]-2-methyl-1-phenyl-dec-1-ene and 4-[(*tert*-butyldimethylsilyl)oxy]-2-methyldec-1-ene in 20% and 30% yield, respectively. The hydrocarbon which results from adventitious protonation is not recyclable. See: Negishi, E.-i.; Okukado, N.; King, A. O.; Horn, D. E. V.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254–2256.

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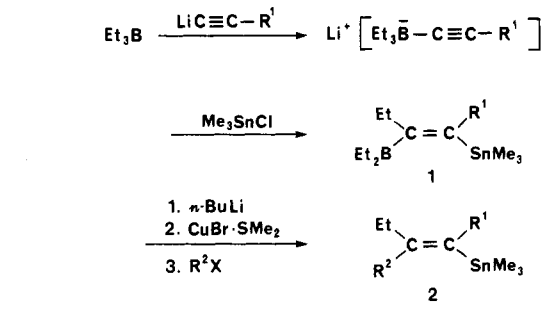
Regio- and Stereoselective Synthesis of Trisubstituted Vinylstannanes

Summary: The selective transformation of the alkenylborane moiety of 1 to alkenylcopper followed by coupling with alkyl halides afforded trisubstituted vinylstannanes with high regio- and stereoselectivity.

Sir: The trialkyltin chloride induced intramolecular transfer reaction of lithium 1-alkynyltrialkylborates was found to be stereoselective with the resulting olefinic intermediate 1 having the migrating alkyl group trans to the trialkyltin group[1-3] (Scheme I). Subsequent protonolysis, oxidation, or iodination afforded the corresponding (*Z*)-alkenes, ketones, or alkynes, respectively.[3] We have adopted these reactions for the synthesis of three straight-chain insect sex pheromones.[3] Interestingly, reactions of 1 with alkynylstannanes have also been observed.[2b] However, the olefinic intermediate 1 constructed with both boron and tin substituents has not been fully explored for other synthetic applications. We believe that this bifunctional intermediate could provide many synthetic opportunities and wish to report our recent findings in this area.

Scheme I



Scheme II

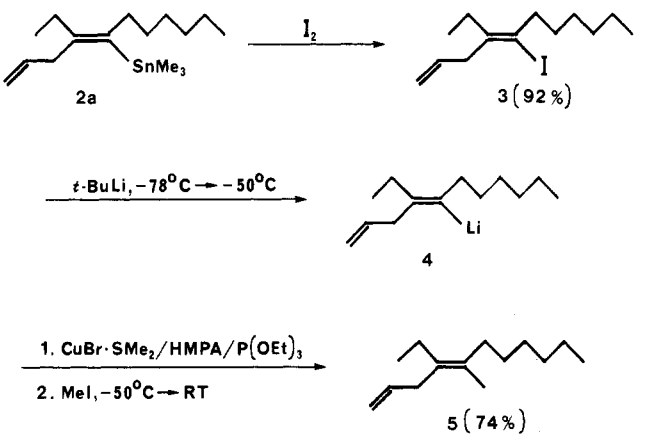


Table I. Preparation of Trisubstituted Vinylstannanes

vinylstannane	R^1	R^{2a}	isolated yield,[b] %
2a	n-C_6H_{13}	$H_2C{=}CHCH_2$	80
2b	n-C_6H_{13}	CH_3	70
2c	$CH_2CH_2CH_2Cl$	$H_2C{=}CHCH_2$	75
2d	C_6H_5	$H_2C{=}CHCH_2$	58
2e	CH_2SiMe_3	$H_2C{=}CHCH_2$	61

[a] R^2X = allyl bromide or methyl iodide. [b] The isolated products have been fully characterized by IR and ^1H and ^{13}C NMR (JEOL GX-270, 270 MHz in ^1H) spectroscopy and satisfactory carbon (±0.22%) and hydrogen (±0.21%) composition determined by combustion analysis.

It has been shown that both alkenylboranes and alkenylstannanes can be converted to alkenylcopper derivatives by first treating with an alkyllithium reagent followed by adding the resulting solution to a copper(I) species.[4,5] We found that the dialkylborane moiety of 1 could be selectively reacted with an alkyllithium reagent without interference from the adjacent trimethyltin group.[6] The resulting alkenylcopper derivative was then coupled with allyl bromide or methyl iodide to form the corresponding trisubstituted vinylstannane 2 (Scheme I).

The products summarized in Table I were found to contain only one stereoisomer (>98%) as indicated by the ^1H and ^{13}C NMR spectra (270 MHz in ^1H). Protonolysis of the trisubstituted vinyltin **2b** with 4 N hydrochloric acid produced (*Z*)-3-methyl-3-decene. We have also prepared (*E*)-3-methyl-3-decene by Normant's procedure[7] and have

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(3) Wang, K. K.; Chu, K.-H. *J. Org. Chem.* **1984**, *49*, 5175–5178.

(4) (a) Yamamoto, Y.; Yatagai, H.; Maruyama, K.; Sonoda, A.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1977**, *99*, 5652–5656. (b) Campbell, J. B., Jr.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 549–550.

(5) Piers, E.; Yeung, B. W. A. *J. Org. Chem.* **1984**, *49*, 4567–4569.

(6) The selective reaction of the alkenylborane moiety has also been observed previously with the less nucleophilic (thiomethoxymethyl)lithium.[1]

0022-3263/86/1951-0767$01.50/0