N18 and one of the spiro ring atoms. The actual atom in the spiro ring bonded to N18 was identified by difference NOE experiments (Figure 1). The two C17 proton signals could be assigned as pseudo-axial and pseudo-equatorial from their vicinal coupling constants (axial 6.8 and 12.6 Hz, equatorial 3.3 and 7.6 Hz). Low-power cycled irradiation[7] of the pseudo-equatorial proton multiplet gave a significant enhancement (4.5%) of a one-proton triplet at 4.35 ppm (the reverse enhancement, 2%, was also observed). This proton was vicinally coupled to protons of a methylene group, which showed no further coupling, and whose carbon resonated at 30.27 ppm. These observations could only be accommodated in the discorhabdin skeleton by a C2-N18 bond. The remaining proton signal was at 6.07 ppm, similar to that of CH4 of discorhabdin B (**3**). The full structure of discorhabdin D was proposed as **4**.

A Drieding model of this structure showed features in accord with other NMR evidence. The H-C-C-H dihedral angles were consistent with the vicinal couplings observed. Long-range coupling (ca. 1 Hz) was observed between H4 and H2, and between H4 and H7α, shown by the model to be cases of "a planar zig-zag arrangement".[8] Difference NOE spectra with irradiation of the signals of H1R and H2, the protons closest to H4 in the model, showed slight enhancements (0.5 and 0.8%) of the H4 signal (Figure 1).

Discorhabdins A, B, and C are powerful cytotoxins with IC_{50} values against the P388 cell line in the range 0.03-0.01 μg/mL but in the in vivo P388 model were found to be inactive (T/C <120%).[2] Discorhabdin D had a lower in vitro activity against P388 (IC_{50} 6 μg/mL) but in contrast was considered to have significant[9] in vivo P388 activity (T/C 132% at 20 mg/kg). Mode of action and structural modification studies are under way to ascertain the loci of biological activity in this series.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded on a Varian XL300 spectrometer. Chemical shifts are given in ppm on the δ scale, referenced to the solvent peaks: CHD_2OD at 3.30 ppm in CD_3OD, $(CHD_2)_2SO$ at 2.60 ppm, and $(CD_3)_2SO$ at 39.60 ppm in $(CD_3)_2SO$. UV spectra were recorded on a Varian DMS 100 UV/vis spectrometer. [α] measurements were made on a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on VG7070F or VG7070E mass spectrometers. The IR spectrum was recorded on a Pye Unicam SP3-300 spectrometer as a KBr disk.

Isolation from *L. brevis*. Specimens were collected by SCUBA diving at depths of about 30 m from the Sugar Loaf Islands, Taranaki, New Zealand, in March, 1985. Voucher specimens 5NP3-1 and 5NP5-7 have been deposited in the University of Canterbury Marine Collection. The sponges (320 g) were blended and extracted with CH_3OH and CH_3OH/toluene (3:1) to give, after removal of solvents, a green gum (19 g). This was partitioned on a reverse phase (RP) column[10] to give a combined fraction (2.5 g) containing largely discorhabdin A (**2**). Preparative RPLC (Merck Lobar RP-8 column, 310 × 25 mm; 4 mL/min CH_3OH/H_2O (with 0.05% CF_3COOH) (3:7); 254 nm detection) on a subsample (70 mg) gave initially **4** (4 mg) followed by **2** (31 mg). Further preparative RPLC gave pure **4**, which showed a deep green spot at R_f 0.5 on silica gel TLC (Merck DC-Plastikfolien Kieselgel 60 F_{254}, developed with Et_3N/CH_3OH/CH_2Cl_2 (0.1:1:4)). Under these TLC conditions **2** gave a red-green spot at R_f 0.7.

Isolation from *Prianos* sp. Specimens were collected by SCUBA diving from the legs of Aquapolice, a floating building at Ocean EXPO Park, Okinawa in June, 1986. A voucher specimen, RS-39, has been deposited with Dr. Hoshino. The sponge (1.8 kg) was extracted by steeping in acetone (6 L) for 2 days. After removal of the acetone the aqueous suspension was extracted with ethyl acetate (2 × 500 mL) to give, after removal of the solvent, a green oil (4 g). A portion of the oil (910 mg) was separated into 12 fractions by centrifugal counter current chromatography using the system $CHCl_3/CH_3OH/H_2O$ (5:5:6) with the upper phase as the mobile phase. Fractions 7 and 8 (96 mg) were further purified on silica gel ($CHCl_3/CH_3OH$; 2:1) to give **4** as a green solid. Repeated purification of fractions 9-12 (165 mg) on silica gel ($CHCl_3/CH_3OH$; 3:1) gave **2** (40 mg), also as a green solid. **2** and **4** from the *Prianos* sp. were identical with the samples from *L. brevis* by spectral comparison.

Discorhabdin D (4) was characterized as its hydrochloride salt, a deep green solid, mp >360 °C; $[\alpha]_D$ 0°, $[\alpha]_{578}$ -45°, $[\alpha]_{546}$ -160° (*c* 0.15, CH_3OH). HRFABMS: MH^+ found 336.08208, calcd for $C_{18}H_{14}N_3O_2S$ 336.08069. UV (CH_3OH): 248 nm (log ϵ 4.35), 281 (4.15), 320 (3.93), 395 (3.95), 584 (2.84). UV (CH_3OH/KOH): 362 nm (log ϵ 4.49), 290 (4.19), 368 (3.98). IR: 3700-2300, 1650, 1620, 1550, 1525, 1490, 1410, 1310 cm^{-1}. ^{1}H NMR (CD_3OD): δ 7.10 (d, J = 1.0 Hz, H14), 6.07 (t, 0.8, H4), 5.60 (dd, 1.4, 3.4, H8), 4.35 (t, 2.8, H2), 4.0 (ddd, 3.3, 7.6, 14.3, H17α), 3.9 (ddd, 6.8, 12.6, 14.3, H17β), 3.2 (dddd, 1.1, 7.8, 12.5, 16.9, H16α), 3.1 (ddd, 3.2, 7.2, 16.6, H16β), 2.91 (dd, 2.8, 13.5, H1R), 2.80 (dd, 3.6, 11.9, H7β), 2.64 (dd, 1.3, 12.1, H7α), 2.58 (dd, 3.1, 13.3, H1S). ^{1}H NMR ($\{CD_3\}_2SO$): δ 13.45 (s, NH13), 10.8 (s, NH9), 7.37 (s, H14), 6.22 (s, H4), 5.79 (s, H8), 4.47 (s, H2), 4.13 (m, H17α), 3.92 (m, H17β), 3.15 (m, H16), 3.02 (d, 12.8, H1R), 2.80 (d, 12.8, H7β), 2.65 (d, 12.8, H7α), 2.55 (d, 12.8, H1S). ^{13}C NMR ($\{CD_3\}_2SO$): δ 183.08 (s, C3), 173.14 (s, C5), 166.47 (s, C11), 147.84 (s, C10 or C19), 145.90 (s, C19 or C10), 127.00 (d, $^1J_{CH}$ = 190 Hz, C14), 123.69 (s, C12 or C21), 121.50 (s, C21 or C12), 117.71 (s, C15), 112.43 (d, 168, C4), 99.64 (s, C20), 62.79 (d, 169, C8), 62.26 (d, 159, C2), 51.24 (t, 145, C17), 41.19 (s, C6), 38.59 (t, C7), 30.27 (t, 137, C1), 19.49 (t, 134, C16). **4** showed antimicrobial activity (at 30 μg/disk) against *Escherichia coli*, *Bacillus subtilis*, and *Candida albicans*, but not against *Pseudomonas aeruginosa*.

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Titanium-Induced Reductive Elimination of 2-Yne-1,4-diols

Jiling Huang,[1] V. Goedken, and H. M. Walborsky*

Dittmer Laboratory of Chemistry, Florida State University, Tallahassee, Florida 32306-3006

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It has been shown that a low-valent titanium surface (Ti(0); Ti (II)) provides a good electron source capable of donating electrons to suitable substrates by a two SET mechanism.[2,3] A good substrate is one with an "electron

(1) Visting scholar from the Shanghai Institute of Organic Chemistry, Academia Sinica.

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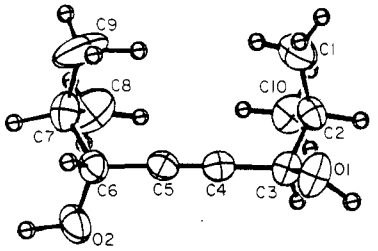


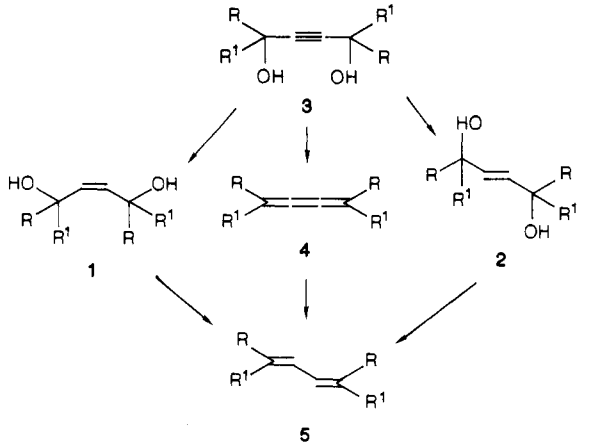
Figure 1. ORTEP plot of *threo*-2,7-dimethyl-4-octyne-3,6-diol.

sink" such as a π-electron system, namely a carbonyl, aryl, or olefinic group. In the case of aryl or olefinic groups an oxygen atom, in the form of alcohol or ether, should be on an adjacent carbon atom. The oxygen atom is converted to a leaving group by the coordination of the oxyphilic titanium with an *n*-bonding pair of electrons on oxygen. Thus, benzyl alcohol can be coupled to bibenzyl[4] or allyl alcohol to bially,[5] 1,3-dimethoxy or 1,3-diols possessing an aromatic ring in the 1- or 3-position, to cyclopropanes,[3,6] and ketones coupled to yield pinacols or olefins.[7-9] It is in this manner that reductive coupling or reductive elimination is achieved by low-valent titanium.

The demonstration that *cis*- or *trans*-2-ene-1,4-diols and their mono or dimethyl ether derivatives can undergo reductive elimination with low-valent titanium to yield 1,3-dienes is of special interest.[10] Due to the ease of preparation of 2-ene-1,4-diols, this reaction holds promise of becoming a convenient and general method for the preparation of 1,3-dienes. Indeed, the reaction has recently been used by Solladie and Hutt[11] as the key step in their elegant total synthesis of dihydrovitamin DHV_3 and dihyrotachesterol DHT_3.

Since the precursors for the preparation of the *Z*-(**1**) or *E*-2-ene-1,4-diols (**2**) are the 2-yne-1,4-diols (**3**) one wondered whether the acetylenic diols themselves could be used directly to produce 1,3-dienes. Thus, in order to address this question the titanium-induced reductive elimination of bis(1-hydroxycyclohexyl)acetylene (**3**, R, R^1 = $(CH_2)_5$), 2,5-dimethyl-3-hexyn-2,5-diol (**3**, R = R^1 = CH_3), and *erythro*- and *threo*-2,7-dimethyl-4-octyn-3,6-diol (**3**, *R* = isopropyl, R^1 = H) was investigated.

The preparation of **3** simply involves the condensation of a metalloacetylide with the appropiate aldehyde or ketone, a reaction which has been amply reviewed.[12,13]



Compound **3** (R = isopropyl, R^1 = H) deserves comment. The condensation of isobutyraldehyde with acetylenebis(magnesium bromide) leads to a mixture of *erythro*- and *threo*-2,7-dimethyl-4-octyn-3,6-diol.[13] We have established by X-ray analysis (Figure 1) that the higher melting isomer, mp 108–109 °C, has the threo configuration and therefore the lower melting isomer (64–65 °C) has been assigned the erythro configuration.

Although we had shown[10] that the reaction of 1,1,4,4-tetraphenyl-1,4-dihydroxy-2-butyne with low-valent titanium yielded only 1,1,4,4-tetraphenyl-1,2,3-butatriene (**4**, R = R^1 = phenyl), it was felt that this was a special case, since the resultant cumulene was highly stabilized and would therefore resist further reduction. Indeed, under the same conditions the reaction of 2,5-dimethyl-3-hexyne-2,5-diol (**3**, R = R^1 = CH_3) gave a 69% yield of reductive elimination product consisting of 90% desired diene **5** (R = R^1 = CH_3) and 10% of a 1:1 mixture of (*E*)- and (*Z*)-2,5-dimethyl-3-hexene. A similar result was obtained with bis(1-hydroxycyclohexyl)acetylene (**3**, R, R^1 = $(CH_2)_5$). The yield, based on recovered starting material, was 90% and consisted of 63% 1,3-diene **5** (R, R^1 = $(CH_2)_5$), 20% (*E*)-1,2-dicyclohexylethylene, and 10% of the *Z* isomer. Under the reaction conditions, the 1,3-diene **5** (R, R^1 = $(CH_2)_5$), once formed, is stable. This was demonstrated by treating the 1,3-diene under conditions identical with those used for the reductive elimination reaction and recovering the unreacted diene in >98% yield. In a similar experiment it was also shown that the *E*/*Z* ratio of the olefins did not change as well.

We had postulated that the 2-yne-1,4-diols (**3**) yielded 1,3-dienes (**5**) as well as olefinic products by initially forming a comulene intermediate (**4**). The cumulene **4** (R = R^1 = CH_3) was therefore prepared and subjected to reaction with low-valent titanium. The reaction produced, as expected, an 80% yield of 1,3-diene **5** (R = R^1 = CH_3) as well as trace amounts of olefins.[14]

In order to gain some insight into the stereochemistry of the reductive elimination reaction, *erythro*- and *threo*-2,7-dimethyl-4-octyne-3,6-diol were subjected to reaction with low-valent titanium. Both stereoisomers yielded identical products, showing that the reaction was not stereospecific. This suggests that the reductive elimination gives rise to a mixture of *Z* and *E* cumulenes, **6** and **7**, respectively, which upon subsequent reduction yields a mixture of 1,3-dienes and olefin products.

The reduction of *threo*-2,7-dimethyl-4-octyne-3,6-diol gave an 88% yield of reaction products, 50% of which consisted of a mixture of (*Z*)- and (*E*)-2,7-dimethyl-4-

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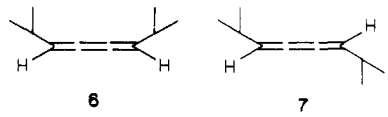

6 7

octene (1:4) and 50% of a 1,3-diene mixture of geometric isomers composed of *EZ*, *ZZ*, and *EE* in a ratio of 3.3:1:1, respectively. The erythro isomer gave an identical mixture of products.

In summary, it has been shown that 2-yne-1,4-diols react with low-valent titanium to yield largely 1,3-dienes with a minor product consisting of olefins. The reductive elimination reaction of 2-yne-1,4-diols is not a stereospecific reaction.

Experimental Section

Infrared (IR) spectra were measured with Perkin-Elmer Model 257 grating spectrophotometer with use of a polystyrene 1601-cm^{-1} bond for calibration. Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ solution unless specified otherwise at 200 or 270 MHz. For flash chromatography, silica gel (40 μm) (Baker) was used unless noted otherwise. Radial chromatography separations were performed with Merck silica gel 60 PF_{254} by using an Harrison Research Chromatotron Model 7924T.

The starting materials were prepared following the reported procedures.[13,16,17] Analytically pure samples of *erythro*- (mp 64–65 °C, lit.[13] mp 65–68 °C) and *threo*- (mp 108–109 °C, lit.[13] mp 104–105 °C) 2,7-dimethyl-4-octyn-3,6-diols were obtained by recrystallization from hexane.

Reaction of Bis(1-hydroxycyclohexyl)acetylene (3, R, R^1 = $(CH_2)_5$). A suspension of 3.7 g (24 mmol) of $TiCl_3$ in 60 mL of dry THF was cooled to 0 °C, and then 445 mg (12 mmol) of $LiAlH_4$ was added in small portions. The resulting black suspension was stirred for 30 min without an ice bath, and the mixture was heated at reflux for an additional hour. The reaction mixture was cooled to 0 °C, 1.33 g (6 mmol) of **3** (R, R^1 = $(CH_2)_5$) was added, stirring was continued for 30 min, and the mixture was kept at refluxing temperature for 3 h. To the mixture, cooled to 0 °C, was added 45 mL of 2 N hydrochloric acid. Then, the mixture was extracted with chloroform. The chloroform extract was washed with water and dried over anhydrous magnesium sulfate, and the solvent was removed to yield 1.08 g (90%) of a mixture of primarily three alkenes, which GLC analysis showed to consist of 63% dicyclohexylideneethane.[10,15] The pure sample was obtained by crystallization of the crude mixture following literature procedure:[15] mp 45 °C (lit.[15] mp 45–47 °C); ^1H NMR δ 1.2–1.75 (m, 12 H), 2.1–2.4 (m, 8 H), 6 (s, 2 H); ^{13}C NMR δ 26.93, 27.69, 28.64, 28.91, 37.65 (10 ring CH_2), 117.26 (2 C=*C*H), 140.77 (2 *C*=CH); IR (CCl_4) 1620 cm^{-1}; UV data are identical with that of the reported values;[15] 20% of (*E*)-1,2-dicyclohexylethylene: ^1H NMR δ 0.85–1.95 (m, 22 H), 5.09 (dd, J = 6.2, 2.2, 2.2 Hz, 2H) and 10% of (*Z*)-1,2-dicyclohexylethylene: ^1H NMR δ 0.85–1.95 (m, 22 H), 5.3 (dd, J = 3.6, 1.5 Hz, 2 H).

An authentic mixture of (*E*)- and (*Z*)-1,2-dicyclohexylethylene was prepared by Ti(0) coupling of cyclohexanecarboxyaldehyde according to the procedure of McMurry.[8] The ratio of *E*:*Z* was 1:4 based on ^1H NMR analysis. The ^1H NMR spectrum was identical with that observed from the above reaction. The ratio did not change upon heating this mixture with low-valent titanium for 3 h.

Reaction of 2,5-Dimethyl-3-hexyne-2,5-diol (3, R = R^1 = CH_3). In a manner similar to that described above, 0.93 g (6.5 mmol) of **3** (R = R^1 = CH_3) was treated with low-valent titanium, (4 g (26 mmol) of $TiCl_3$ and 0.48 g (13 mmol) of $LiAlH_4$). Radial chromatography of the crude product, using pentane as eluent, yielded 500 mg (69% based on recovered starting material) of a less polar fraction, which by ^1H NMR data was shown to consist a mixture of 90% 2,5-dimethyl-2,4-hexadiene (identical (^1H NMR) with an authentic sample, Aldrich), and 5% each of two olefins. On the basis of the ^1H NMR data from this mixture: δ 0.98 (d, 12 H), 2.22 (m, 2 H), 5.31 (dd, J = 4.4 Hz, 2 H), and 0.95 (d, 12 H), 2.65 (m, 2 H), 5.05 (dd, J = 6.5 Hz, 2 H), the two minor olefins were tentatively identified as (*Z*)- and (*E*)-2,5-dimethyl-3-hexene, respectively.

Reaction of 2,5-Dimethyl-2,3,4-hexatriene (4, R = R^1 = CH_3). Under previously described conditions, 500 mg (4.6 mmol) of **4** (R = R^1 = CH_3)[16] was treated with low-valent titanium (2.9 g (18 mmol) of $TiCl_3$ and 0.34 g (9.2 mmol) of $LiAlH_4$) to yield upon workup 401 mg of product, 2,5-dimethyl-2,4-hexadiene and trace amounts of (*E*)- and (*Z*)-2,5-dimethyl-3-hexene.

Reaction of *threo*-2,7-Dimethyl-4-octyne-3,6-diol (3, R = isopropyl, R^1 = H). In a manner similar to that described for the other 2-yne-1,4-diols, 1.03 g (6 mmol) of **3** (R = isopropyl, R^1 = H) was treated with low-valent titanium (3.7 g (24 mmol) of $TiCl_3$ and 445 mg (12 mmol) of $LiAlH_4$) to yield upon workup and radial chromatography, separation with pentane, 0.61 g (88% yield based on recovered starting material) of a less polar fraction: HPLC analysis (Ultrasphere-Si column, solvent heptane) showed the presence of five main compounds: IR (CCl_4) 2900 (m), 1630 (w), 1470 (m), 1380 (m), 1170, 1110, 970, 930, 890, and 870 cm^{-1}; GC–MS: 140 (12), 139 (100), 138 (31), 137 (16), 125 (26), 111 (48), 99 (34). Only a partial separation of each compound from this mixture was achieved by repeated flash chromatography with heptane as eluent. From the analyses of ^1H NMR spectral data along with ^1H decoupling experiments for each compound, the following structures have been assigned. The original mixture consisted a 25% of **(*E*)-2,7-dimethyl-4-octene**:[18] ^1H NMR δ 0.89 (m, 12 H), 1.60 (m, 2 H), 1.90 (m, 4 H), 5.41 (m, 2 H). 25% **(*Z*)-2,7-dimethyl-4-octene**: ^1H NMR δ 0.89 (d, 12 H), 1.60 (m, 2 H), 1.92 (dd, 4 H), 5.26 (m, 2 H). 50% of a mixture of dienes in the ratio of 3.3:1:1, identified[19] as **2,7-dimethyl-3(*Z*),5-(*E*)-octadiene**: ^1H NMR δ 0.8–1.2 (CH_3 doublets, 12 H), 2.30 (m, 1 H, C_2-H), 2.78 (m, 1 H, C_7-H), 5.14 (t, 1 H, J = 10, C_3-H), 5.62 (dd, 1 H, J = 7, 15, C_6-H), 5.82 (t, 1 H, J = 10, C_4-H), and 6.26 (m, 1 H, J = 1, 10, 15, C_5-H). **2,7-Dimethyl-3(*Z*),5(*Z*)-octadiene**: ^1H NMR δ ~0.95 (CH_3 doublets, 12 H), 2.3 (m, 2 H, 2 C*H*(CH_3)$_2$), 5.25 (br t, 2 H, J = 10, C_3-H and C_6-H), and 6.14 (br d, 2 H, J = 2, 10, C_4-H, and C_5-H). **2,7-Dimethyl-3(*E*),5-(*E*)-octadiene**: ^1H NMR δ ~1 (CH_3 doublets, 12 H), 2.78 (m, 2 H, 2 C*H*(CH_3)$_2$), 5.54 (dd, 2 H, J = 6, 12, C_3-H and C_6-H), and 5.97 (m, 2 H, J = 1, 3, 12, C_4-H and C_5-H).

Details of X-ray Data Collection, Structure Determination, and Refinement for *threo*-2,7-Dimethyl-4-octyne-3,6-diol. Single crystals of $C_{10}H_{18}O_2$ were grown by slow evaporation of a saturated petroleum ether solution. The crystals, mp 108–109 °C, were orthorhombic, space group PbCa with a = 8.925 (3) Å, b = 11.302 (8) Å, c = 21.220 (3) Å, and d_{calcd} = 1.206 g cm^{-3} for Z = 8 (M_r = 194.28). The intensity data were measured on a CAD4 Enraf Nonius Diffractometer (Mo radiation, monochromated, θ–2θ scans). The size of the crystal used for collection was approximately 0.30 × 0.25 × 0.30 mm^3. No absorption correction was necessary (μ = 0.78). A total of 2196 reflections were measured for $2\theta \leq 50°$, of which 1112 were considered to be observed [$I > 2\sigma(I)$]. The structure was solved by direct methods with MULTAN 78 (Main, Peter *MULTAN 78. A system of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*; Department of Physics, University of York, York, England. All computations were performed on a PDP 11/34 computer with the aid of the Structure Determination crystallographic program library obtained with the purchase of the X-ray equipment) and refined by full-matrix least-squares methods. In the final refinement anisotropic thermal parameters were used for non-hydrogen atoms. Methyl and hydroxyl hydrogen atoms were located from a difference Fourier map; the remaining hydrogen atom parameters were calculated, assuming idealized geometry. Hydrogen atom contributions were included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices were R = 0.062 and R_W = 0.068 for the 1112 observed reflections. The final difference

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(17) Dehmlow, E. V., Shamout, A. R. *Ann. Chem.* **1982**, 1750.

(18) The *E*/*Z* assignments have been tentatively made on the qualitative observation that the coupling for the *E* olefin at 5.41 ppm appeared to be larger than that for the *Z* isomer at 5.26 ppm in the decoupled spectra.
(19) Albriksten, P.; Cunlifle, A. V.; Harris, R. K. *J. Magn. Reson.* **1970**, *2*, 150.

Fourier map was essentially featureless with no peaks greater than 0.3 e A^{-3}.

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Supplementary Material Available: Crystal data, interatomic distances, and selected bond angles (2 pages). Ordering information is given on any current masthead page.

Efficient Preparation of [(Methoxymethoxy)methyl]tributylstannane, a Convenient Hydroxymethyl Anion Equivalent

Carl R. Johnson* and John R. Medich

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

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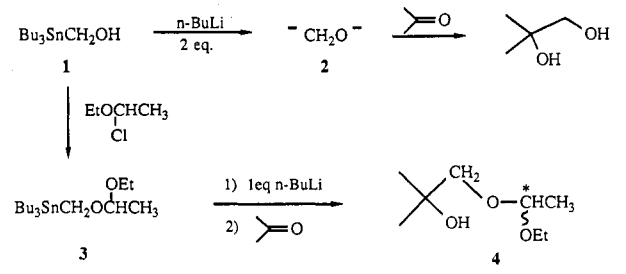
The utility of α-alkoxy organostannanes as precursors to α-alkoxy organolithiums has been demonstrated by several groups.[1] Recently Macdonald, McGarvey, and co-workers published a detailed study of the tin–lithium exchange process of this class of compounds and demonstrated the utility of tertiary α-alkoxy organostannanes for the formation of highly substituted, functionalized carbon–carbon bonds.[2] Primary α-alkoxy organostannanes[3] have been used by several investigators as hydroxymethyl anion equivalents.[4] The direct hydroxymethylation of carbonyl compounds was achieved by Seebach and Meyer,[3a] who treated (tributylstannyl)methanol (1) with 2 equiv. of *n*-BuLi to produce the dianion **2** of methanol. The dianion added to carbonyl compounds to give diols directly (Scheme I). The utility of this method, however, is limited due to the instability of the reagent and the moderate yields of addition products. Still extended the utility of **1** by protecting the free alcohol by using α-chloroethyl ethyl ether to give the stable ethoxyethyl ether **3**.[3b] Compound **3** upon treatment with 1 equiv, of *n*-BuLi gave the α-alkoxy organolithium, which added in high yield to carbonyl compounds, providing monoprotected diols **4**.

In the context of some target molecule syntheses currently under way in our laboratory, the presence of a chiral center in **3** along with its introduction into products of type **4** was disadvantageous. The related MOM derivative **5** was foreseen as fulfilling our need of an acid-sensitive protecting group, which would not introduce new diastereomers. Compound **5** has been recently prepared by McGarvey by alkylation of **1** with chloromethyl methyl ether. For the synthesis of **5** we sought an efficient and cost-effective route that avoided the use of the toxic chloromethyl methyl ether. The results of our investigation are presented here.

For the preparation of (tributylstannyl)methanol (**1**), we used the method described by Still,[3b] in which lithium diisopropylamide (LDA) is used to deprotonate tributyltin hydride. The resulting (tributylstannyl)lithium was treated with paraformaldehyde to give **1**.[5] Methoxymethylation of the crude alcohol **1** was carried out by using

Scheme I



Scheme II

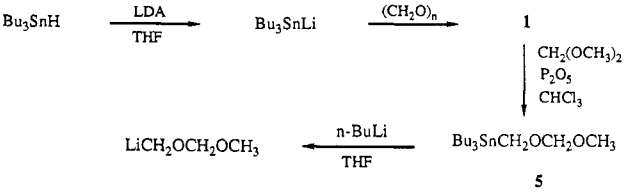
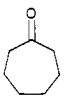
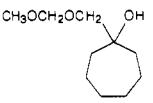
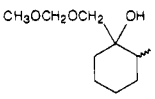
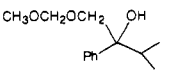
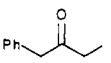
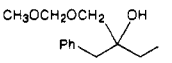
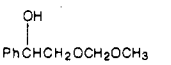
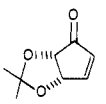
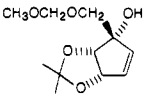
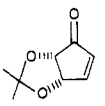
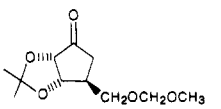
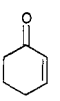
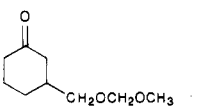
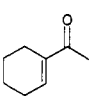
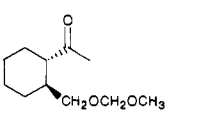


Table I. Addition of α-Alkoxy Stannane 5 to Carbonyl Compounds

entry	substrate	procedure	product	yield,[a] %
1		A		93
2		A		95
3		A		94
4		A		96
5	PhCHO	A		96
6		A		96
7		B		70
8		B		53 (82)[b]
9		B		35 (92)[b]

[a] Isolated yield of pure product. [b] Based on recovered starting material.

(1) (a) Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron Lett.* **1987**, *28*, 3911. (b) Linderman, R. J.; Godfrey, R. J. *Ibid.* **1986**, *27*, 3911. (c) Duchene, A.; Quintard, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 29.

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(3) (a) Seebach, D.; Meyer, N. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 438. (b) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

(4) For other hydroxymethyl anion equivalents, see: (a) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3165. (b) Imamoto, T.; Takayama, T.; Yokoyama, M. *Ibid.* **1984**, *25*, 3225. (c) Tamao, K.; Ishida, N. *Ibid.* **1984**, *25*, 4245.

(5) We explored a number of other methods for preparing tributyltin anion, all of which were found to be inferior to the LDA method; see: (a) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237. (b) Lahournere, J. C.; Valade, J. *C. R. Seances Acad. Sci., Ser. C* **1970**, *C270*, 2080. (c) Corriu, R. J. P.; Guerin, C. *J. Organomet. Chem.* **1980**, *197*, C19.

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