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Syntheses of Stereodefined β-Alkylidene-γ-Lactones and Substituted β,γ-Unsaturated δ-Lactones†

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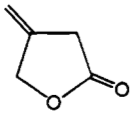
ABSTRACT

1-Trimethylsilyl-1,3-diyne derived trans-bis(trimethylstannyl)enynes undergo stepwise transmetallation with methyllithium to furnish the corresponding enynyllithium reagents. The application, in various orders, of a sequence of transmetallation-protonation-alkylation-hydroxyalkylation-hydroboration-oxidation reactions provides a novel approach to stereo-defined β-alkylidene γ-lactones and β, γ-unsaturated δ-lactones.

INTRODUCTION

α-Alkylidene-γ-lactones [1], γ-alkylidene-γ-lactones [2] and α, β-unsaturated δ-lactones [3] occur widely in nature as building blocks for many natural products, especially the sesquiterpene lactones. These exhibit a wide range of biological activities, which has resulted in a high level of interest in the development of novel synthetic routes for their preparation. Although the β-methylidene-γ-butyrolactone **1** and the β, γ-unsaturated δ-valerolactone **2** structural features are also encountered in a number of natural products [4], methods currently available for their preparation are confined to simple lactone structures [5].



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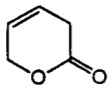

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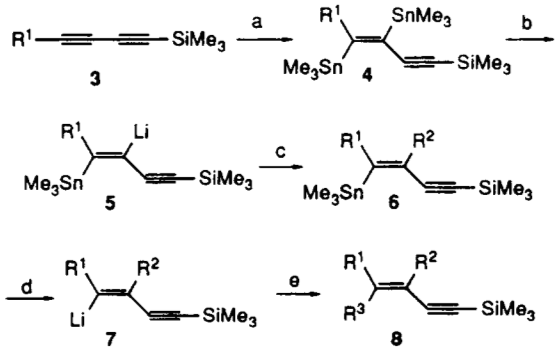
Recently we reported that treatment of 1-trimethylsilyl-1,3-diynes **3** with (trimethylstannyl)copper in THF solvent furnishes chemo- and stereospecifically the corresponding (*E*)-bis(trimethylstannyl)enynes **4**. These undergo selective transmetallation with methyllithium in THF to give the lithiated enynylstannanes **5**. Protonation or alkylation of these produces the mono-enynylstannanes **6** which, upon treatment with methyllithium in DME (dimethoxyethane) solvent, afford the enynyllithiums **7**. Their protonation or alkylation provides stereodefined trisubstituted and tetrasubstituted enynes **8** (eq 1) [6].



(1)

R^1 = alkyl; R^2, R^3 = H or alkyl

(a) $Me_3SnCu\text{-}SMe_2 \cdot LiBr$ [2 equiv]; (b) MeLi / THF / Et_2O; (c) MeOH or R^2I; (d) MeLi / DME / Et_2O (e) MeOH or R^3I

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†Dedicated with great admiration to Professor Herbert C. Brown on the occasion of his 80th birthday.

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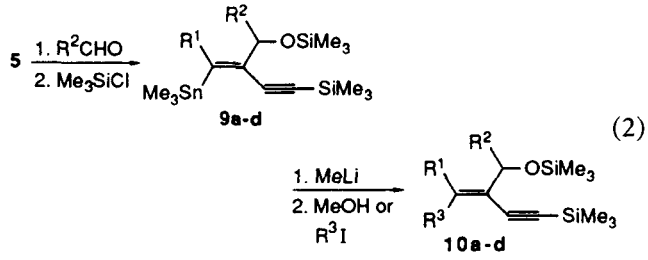
An important aspect of our ongoing research on the synthetic utility of bis(trimethylstannyl)enynes **4** as intermediates in organic synthesis is their elaboration into various functionally substituted enynes of predictable stereochemistry. We now wish to report that bis(stannyl)enynes **4** may be converted stereoselectively into β-alkylidene-γ-lactones and β,γ-unsaturated δ-lactones.

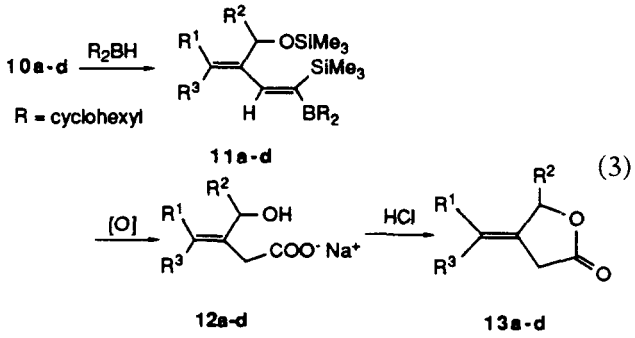
RESULTS AND DISCUSSION

Treatment of 1-(trimethylsilyl)-1, 3-diyne [7] derived bis(stannyl)enynes **4** [6] in THF solvent with 1 equiv. of methyllithium at −78°C results in the selective transmetallation of the trimethylstannyl moiety at C-3. Hydroxyalkylation of the enynyllithium **5** formed with an aldehyde, followed by trapping the lithium alkoxide with chlorotrimethylsilane, produces the silyloxy stannylenyne **9** (eq 2). Destannylation of **9** is achieved by replacing the THF with DME followed by transmetallation with methyllithium. It should be noted that for the tin-lithium exchange to proceed to completion it is necessary to change the solvent for the transmetallation reaction. The resultant intermediate enynyllithiums are then protonated with methanol to furnish the silyloxy enynes **10a,b** (eq 2). Since the silyloxy enynes prepared in this study were sensitive to hydrolytic cleavage, they were isolated by concentrating the reaction mixture under reduced pressure, extraction of the residue with pentane and chromatography on Florisil.



(2)

Monohydroboration of simple 1−trimethylsilyl-1-alkynes with dialkylboranes proceeds in a highly regioselective manner to produce the corresponding 1-boryl-1-silylalkenes. We have previously shown that oxidation of these with an excess of alkaline hydrogen peroxide followed by acidification of the reaction mixture affords the corresponding carboxylic acids in high yields [8]. Thus, the silyloxy enynes **10a,b** were treated with one equivalent of dicyclohexylborane [9]. The ^{1}H NMR spectrum of the vinyl proton region of the resultant dienylborane **11a** exhibited only one singlet at 6.55 ppm, indicating that the hydroboration of **10a,b** had proceeded in a highly regioselective manner placing the boron at the silicon-substituted carbon of the triple bond. This was confirmed by oxidation of **11** with an excess of alkaline hydrogen peroxide to give the hydroxy carboxylates **12** which were directly acidified with conc. HCl to afford, after workup, the β-alkylidene-γ-butyrolactones **13a,b** (eq 3). The assignment of the (*Z*)-configuration to the lactones is based on the stereoselectivities previously observed [6] in the individual steps leading to the lactones. Interestingly, attempted hydroboration of the unprotected hydroxy enynes



(3)

instead of the silyloxy enynes with 2 equiv. of dicyclohexylborane did not proceed to completion.

The trimethylstannyl group in **9** may not only be replaced by a hydrogen in giving **10**, but it also provides a site for carbon-carbon bond formation. Thus, lithiation of **9c** in DME with methyllithium and trapping the intermediate enynyllithium with methyl iodide furnishes the corresponding silyloxy enyne **10c** (eq 2). This, upon hydroboration, oxidation and lactonization affords the (*Z*)-lactone **13c**. The corresponding (*E*)-lactone **13d** is also accessible using the methyl-substituted silyl diyne **3** ($R^1 = CH_3$) and elaborating it into the silyloxy enyne **9d**. This, upon lithiation, alkylation with *n*-hexyl bromide in diglyme, hydroboration, and lactonization produces **13d**. A summary of the yields of silyloxy enynes **10** and β-alkylidene γ-lactones **13** obtained is shown in Table 1.

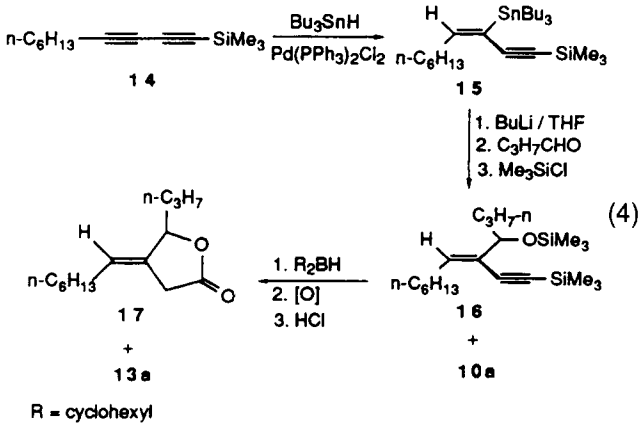
We next explored the possibility of preparing the (*E*)-alkylidene γ-butyrolactone **17**, the stereoisomer of **13a**. An obvious precursor for **17** is the (monostannyl)enyne **15** which is readily available via cis-monohydrostannation of 1-trialkylsilyl-1, 3-diynes **14** with *n*-Bu_3SnH in the presence of $(Ph_3P)_2PdCl_2$ [10]. However, transmetallation of **15** with *n*-BuLi followed by sequential treatment of the resulting enynyllithium with *n*-butanal and chlorotrimethylsilane furnished not only the desired silyloxy enyne **16** but also its isomer **10a** in a 55:45 mixture (eq 4).

Thus, the intermediate enynyllithium formed upon transmetallation of **15** with *n*-butyllithium must be configurationally unstable under the reaction conditions and isomerizes to give, after hydroxyalkylation, a mixture of the (*E*) and (*Z*)-silyloxy enynes **16** and **10a**. In this connection it is worth noting that lithiation of the (*Z*)-enynyl bromide **18** ($R^1 = n\text{-}C_6H_{13}$) with sec-BuLi at −76°C also produces a mixture of (*E*)-and (*Z*)-enynyllithiums, as evidenced by the formation of the enynes **19a** and

TABLE 1. Yields of Enynyl Silyl Ethers **10, 20** and Lactones **13, 22**

Entry	R^1	R^2	R^3	Yield, %[a,b]			
				10	**13**	**20**	**22**
a	n-C_6H_{13}	n-C_3H_7	H	75	85		
b	n-C_6H_{13}	i-C_3H_7	H	73	75		
c	n-C_6H_{13}	C_2H_5	CH_3	73	91		
d	CH_3	C_2H_5	n-C_6H_{13}	69	71		
e	n-C_6H_{13}	H	C_2H_5			71	80
f	CH_3	H	n-C_5H_{11}			74	85
g	n-C_6H_{13}	CH_3	C_2H_5			83	91

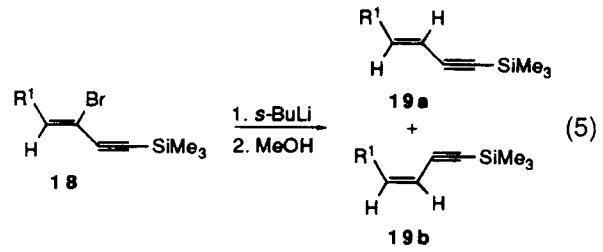
[a] Yields for compounds **10** and **20** are based on the bis(stannyl)enyne **4** and yields for the lactones **13** and **22** are based on the silyloxy enynes **10** and **20**.
[b] It should be noted that the lactones are unstable and must be stored at low temperature.



(4)

19b on methanolysis (eq 5) [11].

It is interesting to contrast the configurational instability of the enynyllithiums derived from the precursors **15** and **18** with the observed stereochemical stability of **5** (vide supra). The reason for the observed geometrical rigidity of **5** may be the result of the additional stability gained through maximum



(5)

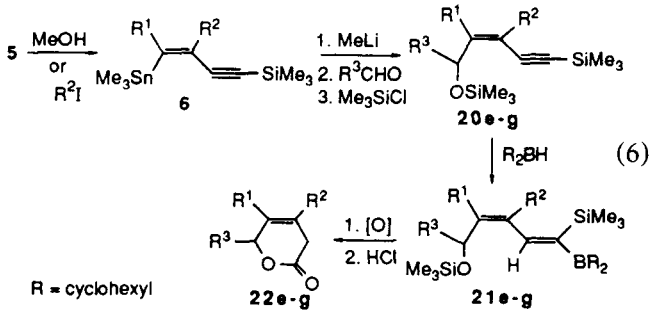
separation of the two olefin attached metal atoms.

To further confirm the structural assignment of the lactones **13** (eq 3), the ^1H NMR data obtained for the pure (*Z*)-lactone **13a** was compared with that for the corresponding (*E*)-lactone. Thus, the silyloxy enyne mixture **16** and **10a** was hydroborated with dicyclohexylborane, then oxidized with alkaline hydrogen peroxide and lactonized to furnish a 55:45 mixture of the lactones **17** and **13a**, respectively. The distinguishing features in the spectra of the two lactones are the different chemical shifts for the absorptions of the ring methylene and methine protons. Thus, the CH_2 protons of (*Z*)-**13a** have different chemical shifts and appear as a broad AB quartet (J = 21.9 Hz) with the lower field doublet at 3.25 ppm having more splitting than the higher field doublet at 3.05 ppm. On the other hand, the CH_2 proton resonances of (*E*)-**17** appear as a broadened singlet at 3.14 ppm. The methine proton resonances of the lactone ring for **13a** and its isomer **17** appear as broad, unresolved absorptions at 5.15 and 4.97 ppm, respectively. The ring CH_2 protons of the (*Z*)-lactone **13b** also exhibited different chemical shifts. However, the lactones **13c** and **13d**, in which the hydrogens at the double bond are replaced by an alkyl group, showed their CH_2 resonances as broad singlets.

The versatility of bis(stannyl)enynes for introducing various substituents onto the enyne system is further evidenced by their conversion into β, γ-unsaturated δ-lactones. Thus, applying the same types of reactions used for the preparation of the five-membered ring lactones **13**, but changing the sequence in which the reagents are added to the bis(stannyl)enyne **4**, afford the nonconjugated β, γ-unsaturated δ-lactones **22**. For example, treatment of **4** (R^1 = n-C_6H_{13}) with methyllithium in THF followed by protonation of the resultant enynyllithium **5** with methanol yielded the mono-stannylenyne **6** (R^2 = H). Alternatively, the enynyllithium reagent **5** may be alkylated with the appropriate alkyl iodide. Replacement of the THF with DME, transmetallation with methyllithium, trapping the resultant enynyllithium with propanal, and addition of chlorotrimethylsilane afforded the silyloxy enyne **20e** (eq 6). Hydroboration of the triple bond in **20e** with one equivalent of dicyclohexylborane furnished a 9:1 mixture of dienylboranes, dominant in the isomer **21** (R^2 = H) having the boron attached at the silicon substituted vinylic carbon. This was evidenced by the presence of a doublet at 6.58 ppm and a singlet at 7.25 ppm in the vinylic region of the ^1H NMR spectra, which integrated for 0.90 H (±0.03) and 0.10 H (±0.03), respectively.

The observed lower regioselectivity in the hydroboration of the silyloxy enyne **20e** as com-

pared to the silyloxy enyne **10a** (eq 2) may be rationalized as follows. Coordination of the trigonal boron of the dialkylborane with the silyloxy group directs the boron to the internal acetylenic carbon of the enynyl moiety. The closer proximity of the silyloxy group to the triple bond in **20e** (eq 6) makes this intramolecular delivery of the B—H bond to the triple bond of the enynyl moiety more likely. A similar explanation has been advanced for the low regioselectivity observed in the hydroboration of (*Z*)-1-methoxy-4-trimethylsilyl-1-en-3-yne with dialkylboranes [12].



Oxidation of the dienylboranes **21e-g** with alkaline hydrogen peroxide furnished the unsaturated six-membered ring lactones **22e-g**. The location of the double bond in the lactones **22** was readily established by integrating the absorptions of the CH_2 and CH protons adjacent to the ring carbonyl and oxygen functions, respectively, in their ^1H NMR spectra. The yields of the silyloxy enynes **20e-g** and of the corresponding lactones **22e-g** are summarized in Table 1.

In conclusion, 1-trimethylsilyl-1, 3-diyne derived *trans*-bis(trimethylstannyl)enynes are valuable intermediates for elaboration into the hitherto not readily accessible five-membered ring β-alkylidene lactones and β, γ-unsaturated six-membered ring lactones. Their chemical properties as well as their biological activities remain to be explored.

EXPERIMENTAL

General Procedures. ^1H NMR spectra were recorded at 300 MHz using $CDCl_3$ as the solvent with the residual chloroform therein serving as the internal standard. ^{13}C NMR spectra were recorded at 75.5 MHz using $CDCl_3$ as the solvent and are referenced to the central triplet peak of $CDCl_3$ at 77.00 ppm. Infrared spectra were recorded on a Perkin-Elmer IR-1310 spectrophotometer. High resolution mass spectra were obtained using a Dupont 21-492B mass spectrometer. The purities of the products obtained were determined by GLC on fused silica capillary (J&W) columns. Elemental analyses were performed by the Microanalytical Laboratory, University of California, Berkeley, California.

Ether, tetrahydrofuran, 1, 2-dimethoxyethane (DME) and diglyme were distilled from sodium and benzophenone immediately prior to use. The glassware for reactions involving organometallic reagents were oven-dried at 150°C for 6 hours, assembled hot, and cooled under a stream of argon or nitrogen before use. All reactions involving these reagents were stirred magnetically and conducted under atmospheres of argon or nitrogen [15].

*(Z)-1-Trimethylsilyl-3-(1'-trimethylsilyloxy-1'-butyl)-3-decen-1-yne (***10a***)*

To a solution of (*E*)-1-trimethylsilyl-3,4-bis(trimethylstannyl)-3-decen-1-yne **4** [6] (4.8 g, 9.0 mmol) and anhydrous THF (18 mL) maintained at −78°C was added 6.8 mL of a 1.32 M solution of methyllithium (9.0 mmol, low halide) in ether. The mixture was stirred for 1 hour at −78°C, the resultant lithiated enyne was treated with *n*-butanal (0.65 g, 9.0 mmol), stirred for 1 hour at −78°C, gradually warmed to room temperature, and stirred for an additional 1 hour. The mixture was cooled to −78°C, treated with chlorotrimethylsilane (0.98 g, 9.0 mmol), stirred for 15 minutes, warmed to room temperature and then stirred for an additional 2 hours. The volatiles were removed under reduced pressure (2 Torr) and the residue obtained was diluted with DME (18 mL). These operations were carried out with the exclusion of air. To the reaction mixture was added at −78°C a 1.32 M solution of methyllithium (9.9 mmol, low halide) in ether. After 1 hour of stirring at −78°C, the resulting enynyllithium was treated with 3 mL of methanol, stirred for 1 hour at −78°C, warmed to room temperature, and stirred for 1 hour. The volatiles were removed under reduced pressure (2 Torr), the residue was dissolved in pentane (18 mL), the suspension was filtered through a short column of sodium sulfate via a double ended needle, the filtrate was concentrated, and the residue was chromatographed on Florisil using hexane as eluent. Concentration and distillation (Kugelrohr) furnished 2.40 g (75%) of **10a**: bp 85−88°C (0.04 Torr); $n^{24}D$ 1.4610; IR (neat) 2160, 1463, 1462, 1250, 1115, 1085, 845 cm^{-1}; ^1H NMR δ 0.10 (*s*, 9H, $SiMe_3$), 0.17 (s, 9H, $SiMe_3$), 0.92 (t, J = 7.5 Hz, 6H, CH_3), 1.27–1.6 (bm, 10H, CH_2), 2.1–2.2 (m, 4H, C = CCH_2, $OCCH_2$), 4.36 (dd, J = 7.5, 6.0 Hz, 1H, OCH), 5.88 (t, J = 7.0 Hz, 1H, C = CH); ^{13}C NMR δ 0.11 (3 C's), 0.21 (3 C's), 13.90, 14.04, 18.89, 22.58, 28.36, 29.10, 29.19, 31.66, 39.11, 69.08, 92.33, 105.28, 127.75, 139.43; HRMS *m/z* 352.2628 (Calcd for $C_{20}H_{40}OSi_2$, 352.2618). GC examination (30 m DB 210 glass capillary column) revealed the compound was 96% pure.

*(Z)-4-Heptylidene-5-n-propyl-2(3H)-furanone (***13a***)*

To a solution of cyclohexene (0.52 g, 6.3 mmol) in

THF cooled at 0°C was added 1.36 mL of a 2.32 M solution of borane-dimethyl sulfide in THF. This was stirred for 30 minutes at 0°C, warmed to room temperature, and stirred for 30 minutes. To the resultant slurry was added at 0°C **10a** (1.06 g, 3.0 mmol), the mixture was warmed to room temperature, stirred for 2 hours, diluted with 4 mL of methanol, oxidized by addition of 3.0 mL of 6 N aqueous sodium hydroxide followed by dropwise addition of 3 mL of 30 % hydrogen peroxide while maintaining the temperature during the addition between 40 and 50°C. The mixture was vigorously stirred for 30 minutes at ambient temperature, cooled to 0°C, acidified with conc. HCl to a pH of 1 while maintaining the temperature below 5°C, stirred for 15 minutes, warmed to room temperature and stirred for 30 minutes. The two phases formed were separated, the aqueous phase was extracted with pentane (5 × 5 mL), and the combined organic phases were washed once with sat. aq. sodium chloride and dried over $MgSO_4$. The solvents were removed and the residue obtained was distilled (Kugelrohr) to yield 0.57 g (85%) of **13a**: bp 94–97°C (0.01 Torr); $n^{24}D$ 1.4673; IR (neat) 2960, 2925, 2855, 1775, 1460, 1165, 975, 840 cm^{-1}; ^1H NMR δ 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.94 (t, J = 7.5 Hz, 3H, CH_3), 1.2–1.6 (bm, 10H, CH_2), 1.6–1.7 (m, 2H, $OCCH_2$), 1.8–1.9 (m, 2H, C = CCH_2), 3.05 (d, J = 21.9 Hz, 1H, C = $CC\underline{H}_2$ C = O), 3.25 (dt, J = 21.9, 2.1 Hz, 1H, C = $CC\underline{H}_2C$ = O), 5.11 (m, 1H, OCH), 5.38 (m, 1H, C = CH); ^{13}C NMR δ 13.74, 14.02, 17.84, 22.55, 28.23, 28.88, 29.24, 31.63, 34.40, 37.29, 82.10, 125.28, 131.74, 175.45 ; HRMS *m/z* 224.1779 (Calcd for $C_{14}H_{24}O_2$, 224.1776). GC examination (15 m DB 1701 glass capillary column) revealed that the compound was 97% isomerically pure.

(Z)-1-Trimethylsilyl-3-(1'-trimethylsilyloxy-i-butyl)-3-decen-1-yne (**10b**)

Following the procedure for the preparation of **10a**, but using *i*-butyraldehyde, (*E*)-1-trimethylsilyl-3,4-bis(trimethylstannyl)-3-decen-1-yne (3.0 mmol) was converted to **10b** (73%): bp 76–82°C (0.03 Torr); $n^{26}D$ 1.4584; IR (neat) 2155, 1450, 1380, 1255, 1090, 895, 850, 770 cm^{-1}; ^1H NMR δ 0.09 (s, 9H, $SiMe_3$), 0.17 (s, 9H, $SiMe_3$), 0.80 (d, J = 6.6 Hz, 3H, CH_3), 0.89 (t, J = 7.2 Hz, 3H, CH_3), 0.96 (d, J = 6.6 Hz, 3H, CH_3), 1.20–1.44 (bm, 8H, CH_2), 1.86 (m, 1H, $(CH_3)_2C\underline{H}$), 2.08–2.20 (m, 2H, C = CCH_2), 3.93 (d, J = 8.1 Hz, 1H, OCH), 5.92 (t, J = 7.5 Hz, 1H, C = CH); ^{13}C NMR δ 0.12 (3 C's), 0.18 (3 C's), 14.04 (2 C's), 18.80, 19.03, 22.58, 28.73, 29.19, 31.68, 33.62, 75.09, 91.88, 105.98, 126.88, 140.19; HRMS *m/z* 352.2629 (Calcd for $C_{20}H_{40}OSi_2$, 352.2618). GLC examination (30m DB210 glass capillary column) revealed that the compound was 98% isomerically pure.

(Z)-4-Heptylidene-5-i-propyl-2(3H)-furanone (**13b**)

Following the procedure for the preparation **13a**, hydroboration of **10b** (3.0 mmol) followed by oxidation and lactonization furnished (75%) of the lactone **13b**: bp 93–98°C (0.02 Torr); $n^{24}D$ 1.4672; IR (neat) 2960, 2925, 2855, 1775, 1470, 1170, 1005, 975, 850 cm^{-1}; ^1H NMR δ 0.87 (t, J = 7.2 Hz, 3H, CH_3), 0.88 (d, J = 6.9 Hz, 3H, $CHCH_3$), 1.04 (d, J = 6.9 Hz, 3H, $CHCH_3$), 1.15–1.50 (m, 8H, CH_2), 1.85–2.00 (m, 3H, C = CCH_2, OCCH), 3.04 (d, J = 21.6 Hz, 1H, C = CCH_2C = O), 3.22 (dt, J = 21.6, 1.5 Hz, 1H, C = CCH_2C = O), 4.97 (m, 1H, OCH), 5.44 (m, 1H, C = CH); ^{13}C NMR δ 13.91, 15.50, 19.05, 22.50, 28.49, 28.86, 29.27, 31.62, 33.33, 35.20, 86.70, 126.26, 131.26, 175.30; HRMS m/z 224.1763 (Calcd for $C_{14}H_{24}O_2$, 224.1776). GLC examination (15 m DB 1701 glass capillary column) revealed that the compound was 98% isomerically pure.

(Z)-1-Trimethylsilyl-3-(1'-trimethylsilyloxy-1'-propyl)-4-methyl-3-decen-1-yne (**10c**)

To a solution of (*E*)-1-trimethylsilyl-3,4-bis (trimethylstannyl)-3-decen-1-yne **4** [6] (2.67 g, 5.0 mmol) in anhydrous THF (10 mL) maintained at −78°C was added a 1.04 M solution of methyllithium (low halide, 5.0 mmol) in ether. The solution was stirred for 1 hour at −78°C, the resultant lithiated enyne was treated with propanal (0.29 g, 5.0 mmol) at −78°C, the mixture was stirred for 1 hour at −78°C, then gradually warmed to room temperature and stirred for 1 hour. The mixture was then cooled to −78°C, treated with chlorotrimethylsilane (0.54 g, 5.0 mmol), stirred for 15 minutes, warmed to room temperature, and then stirred for 2 hours. The volatiles were removed under reduced pressure (1 Torr) and the residue obtained was diluted with DME (10 mL). These operations were carried out with the exclusion of air. A 1.04 M solution of methyllithium (low halide, 5.5 mmol) was added to the resultant mixture at −78°C. After stirring at −78°C for 1 hour, the enynyllithium formed was treated with methyl iodide (0.78 g, 5.5 mmol), stirred at −78°C for 1 hour, warmed to room temperature, and stirred for 1 hour. The volatiles were removed under reduced pressure (1 Torr) and the residue was dissolved in pentane (10 mL). The suspension was then filtered through a short column of sodium sulfate via a double ended needle, and the filtrate was concentrated and the residue was passed through a Florisil column using hexane as eluent. The collected fractions were concentrated and distilled (Kugelrohr) to yield 1.29 g (73%) of **10c**: bp 89–93°C (0.01 Torr); $n^{26}D$ 1.4662; IR (neat) 2960, 2930, 2860, 2868, 2145, 1470, 1462, 1255, 1105, 1075, 875, 845, 760 cm^{-1}; ^1H NMR δ 0.09 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$), 0.80–0.95 (m, 6H, CH_3),

1.25–1.80 (bm, 8H, CH_2), 1.94 (s, 3H, C=CCH_3) 2.00–2.30 (m, 4H, C=CCH_2, $OCCH_2$), 4.31 (dd, J = 7.2, 6.6 Hz, 1H, OCH); ^{13}C NMR δ 0.24 (3 C's), 0.40 (3 C's), 10.52, 14.05, 21.82, 22.59, 28.17, 29.59, 30.17, 31.72, 33.85, 71.48, 97.96, 104.11, 122.65, 146.24; HRMS *m/z* (M^+-CH_3) 337.2389 (Calcd for $C_{19}H_{37}OSi_2$, 337.2383). GC analysis (30 m DB 210 glass capillary column) revealed that the compound contained three minor impurities.

(Z)-4-(1'-Methyl)heptylidene-5-ethyl-2(3H)-furanone (**13c**)

Following the procedure for the preparation **13a**, hydroboration of **10c** (3.0 mmol) followed by oxidation and lactonization yielded 0.31 g (91%) of **13c**: bp 73–77°C (10^{-3} Torr); n^{24}D 1.4669; IR (neat) 2960, 2925, 2860, 1780, 1460, 1178, 980 cm^{-1}; ^{1}H NMR δ 0.94 (t, J = 7.0 Hz, 3H, CH_3), 1.02 (t, J = 7.5 Hz, 3H, CH_3), 1.3–1.7 (bm, 8H, CH_2), 1.70 (s, 3H, C=CCH_3), 1.75–1.85 (m, 2H, $OCCH_2$), 1.9–2.0 (m, 2H, C=CCH_2), 3.16 (s, 2H, C=CCH_2C=O), 5.17 (dd, J = 7.5, 2.1 Hz, ^{1}H, OCH); ^{13}C NMR δ 8.71, 13.97, 18.87, 22.51, 27.53, 28.72, 29.23, 31.64, 33.10, 33.47, 83.75, 125.51, 131.06, 175.91; HRMS *m/z* 224.1775 (Calcd for $C_{14}H_{24}O_2$, 224.1776). GC examination (15 m DB 1701 glass capillary column) revealed that the compound was 98% isomerically pure.

(E)-1-Trimethylsilyl-3-(1'-trimethylsilyloxy-1'-propyl)-4-methyl-3-decen-1-yne (**10d**)

Following the procedure for the preparation of **10c**, (*E*)-1-trimethylsilyl-3, 4-bis(trimethylstannyl)-3-penten-1-yne [6] (1.39 g, 3.0 mmol) was converted to the enynyllithium, and treated sequentially with propanal and chlorotrimethylsilane. The volatiles were removed under reduced pressure (1 Torr) and the residue obtained was diluted with diglyme (6 mL) instead of DME. These operations were carried out with the exclusion of air. To the resultant mixture was added at −78°C a 1.04 M solution of methyllithium (low halide, 3.3 mmol), stirred at −78°C for 1 hour and then treated with *n*-hexyl bromide (0.54g, 3.3 mmol). The mixture was stirred for 1 hour at −78°C, warmed to room temperature, and stirred for 2 hours and worked up as described for **10c**. Distillation (Kugelrohr) yielded 0.73 g (69%) of **10d**: bp 65–69°C (0.02 Torr); n^{24}D 1.4564; IR (neat) 2955, 2925, 2855, 2140, 1250, 1100, 1060, 1014, 860, 845, 760 cm^{-1}; ^{1}H NMR δ 0.09 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$), 0.79–0.95 (m, 6H, CH_3), 1.25–1.50 (bm, 8H, CH_2), 1.54–1.70 (m, 2H, C=CCH_2), 1.77 (s, 311, C=CCH_3), 2.33 (dt, J = 7.5, 3.0 Hz, 2H, $OCCH_2$), 4.28 (t, J = 7.5 Hz, ^{1}H, OCH); ^{13}C NMR δ 0.21 (3 C's), 0.31 (3 C's), 10.21, 14.00, 18.10, 22.66, 27.58, 29.26, 29.91, 31.75, 37.87, 72.14, 97.51, 103.99, 122.86, 145.99; HRMS *m/z* 352.2590 (Calcd for $C_{20}H_{40}OSi_2$, 352.2618). GC examination (15 m DB 1701 glass capillary column) revealed that the compound was 97% isomerically pure.

(E)-4-(1'-Methyl)heptylidene-5-ethyl-2(3H)-furanone (**13d**)

Following the procedure for the preparation of **13a**, hydroboration of **10d** (3.0 mmol) followed by oxidation and lactonization yielded 0.24 g (71%) of **13d**: bp 84–87°C (0.01 Torr); n^{24}D 1.4712; IR (neat) 2955, 2933, 2860, 1780, 1460, 1178, 980 cm^{-1}; ^{1}H NMR δ 0.87 (t, J = 7.5 Hz, 3H, CH_3), 0.95 (t, J = 7.5 Hz, 3H, CH_3), 1.2–1.5 (bm, 8H, CH_2), 1.61 (s, 3H, C=CCH_3), 1.85–1.9 (m, 2H, $OCCH_2$), 1.9–2.0 (m, 2H, C=CCH_2), 3.12 (s, 2H, C=CCH_2C=O), 5.09 (q, J = 3.0 Hz, 1H, OCH); ^{13}C NMR δ 8.69, 14.01, 17.31, 22.55, 27.23, 27.89, 28.98, 31.68, 32.79, 35.79, 83.95, 125.73, 130.99, 175.94 ; HRMS *m/z* 224.1777 (Calcd for $C_{14}H_{24}O_2$, 224.1776). GC examination (15 m DB 1701 glass capillary column) revealed the compound to be 98% isomerically pure.

(Z)-1-Trimethylsilyl-4-(1'-trimethylsilyloxy-1'-propyl)-3-decen-1-yne (**20e**)

To a solution of (*E*)-1-trimethylsilyl-3,4-bis (trimethylstannyl)-3-decen-1-yne **4** [6] (2.67 g, 5.0 mmol) in THF (10 mL) was added at −78°C a 1.04 M solution of methyllithium (low halide, 5.0 mmol) in ether. The solution was stirred for 1 hour at −78°C, the resultant lithiated enyne was treated with 5.0 mL of a 1.0 M solution of methanol (5.0 mmol) in hexane, the mixture was stirred for 1 hour at −78°C, then gradually warmed to room temperature. The volatiles were removed under reduced pressure (0.5 Torr) and the residue obtained was diluted with DME (10 mL). These operations were carried out with the exclusion of air. To the resultant mixture was added at −78°C a 1.04 M solution of methyllithium (low halide, 5.5 mmol). After stirring at −78°C for 1 hour, the resulting enynyllithium was treated with propanal (0.35 g, 6.0 mmol), stirred at −78°C for 1 hour, warmed to room temperature, and stirred for 1 hour. The mixture was then cooled to −78°C, treated with chlorotrimethylsilane (1.36 g, 12.5 mmol), stirred for 15 minutes, warmed to room temperature, and stirred for an additional 2 hours. The volatiles were removed under reduced pressure (0.5 Torr) and the residue was dissolved in pentane (25 mL). The suspension was filtered through a short pad of sodium sulfate via a double ended needle. The filtrate was concentrated and the residue was chromatographed on a Florisil column using hexane as eluent to furnish 1.20 g (71%) of **20e**: bp 83–86°C (10–3 Torr); n^{26}D 1.4618; IR (neat) 2970, 2935, 2870, 2145, 1465, 1250, 1084, 1058, 1015, 885, 845, 763 cm^{-1}; ^{1}H NMR δ 0.10 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$), 0.87 (t, J = 7.0 Hz, 3H, CH_3), 0.95 (t, J = 7.5

Hz, 3H, CH_3), 1.3–1.7 (bm, 8H, CH_2), 2.0–2.2 (m, 4H, C=CCH_2, $OCCH_2$), 4.78 (t, J = 7.0 Hz, 1H, OCH), 5.29 (s, 1H, C=CH); ^{13}C NMR δ −0.07 (3 C's), -0.02 (3 C's), 10.43, 14.09, 22.52, 28.03, 29.26, 31.74, 74.38, 98.45, 102.71, 104.31, 159.63; HRMS *m/z* 338.2444 (Calcd for $C_{19}H_{38}OSi_2$, 338.2461).

3, 6-Dihydro-5-n-hexyl-6-ethyl-2H-pyran-2-one (**22e**)

Following the procedure for the preparation of **13a**, hydroboration of **20e** (1.74 mmol) followed by oxidation-lactonization afforded 80% of **22e**: bp 86–91°C (10^{-2} Torr, Kugelrohr); IR (neat) 2975, 2950, 2870, 1737, 1462, 1381, 1220, 1056, 1051 cm^{-1}; ^{1}H NMR δ 0.85 (t, J = 7.0 Hz, 3H, CH_3), 0.95 (t, J = 7.5 Hz, 3H, CH_3), 1.25–1.70 (bm, 8H, CH_2), 1.80–1.90 (m, 2H, C = CCH_2), 1.90–2.00 (m, 2H, $OCCH_2$), 3.00 (t, J = 4 Hz, 2H, C=CCH_2CO), 4.74 (dd J = 7.5, 4 Hz, 1H, OCH), 5.29 (t, J = 4 Hz, ^{1}H, C=CH); ^{13}C NMR δ 8.58, 14.03, 22.56, 27.29, 27.36, 28.94, 30.05, 31.61, 32.24, 83.39, 115.32, 137.18, 169.92; HRMS *m/z* 210.1623 (Calcd for $C_{13}H_{22}O_2$, 210.1620).

(Z)-1-Trimethylsilyl-5-trimethylsilyloxy-4-methyl-3-decen-1-yne (**20f**)

Following the procedure for the preparation of **20e**, but using *n*-hexanal (2.3 mmol), (*E*)-1-trimethylsilyl-3, 4-bis(trimethylstannyl)-3-penten-1-yne [6] (0.89 g, 1.92 mmol) in THF (4 mL) was converted to the silyloxy enyne **20f** in 74% yield: bp 69–74°C (0.03 Torr); n^{25}D 1.4549; IR (neat) 2140, 1440, 1380, 1255, 1065, 895, 850, 760 cm^{-1}; ^{1}H NMR δ 0.11 (s, 9H, $SiMe_3$), 0.19 (s, 9H, $SiMe_3$), 0.89 (t, J = 6.9 Hz, 3H, CH_3), 1.25–1.65 (bm, 8H, CH_2), 1.74 (s, 3H, CH_3), 4.84 (dd, J = 7.5, 5.4 Hz, 1H, OCH), 5.28 (s, 1H, C=CH); ^{13}C NMR δ −0.06 (3 C's), −0.02 (3 C's), 13.96, 16.56, 22.66, 25.25, 31.66, 35.71, 72.21, 97.68, 102.41, 105.47, 155.72. HRMS *m/z* 310.2152(Calcd for $C_{17}H_{34}OSi_2$, 310.2148).GLC examination (30m DB 210 glass capillary column) revealed the compound was 96% isomerically pure and contained a minor impurity.

3, 6-Dihydro-5-methyl-6-n-pentyl-2H-pyran-2-one (**22f**)

Following the procedure for the preparation of **13a**, hydroboration of **20f** (1.29 mmol) followed by oxidation-lactonization yielded 85% of **22f**: bp 76–82°C (0.03 Torr); IR (neat) 1730, 1450, 1390, 1220, 1060 cm^{-1}; ^{1}H NMR δ 0.87 (t, J = 6.3 Hz, 3H, CH_3), 1.20–1.90(bm, 11H, CH_2), 3.00 (d, J = 1.2 Hz, 2H, C=CH_2CO), 4.77 (dd, J = 6.3, 2.7 Hz, 1H, OCH), 5.48 (s, 1H, C=CH); ^{13}C NMR δ 13.93, 18.81, 22.45, 23.67, 29.89, 31.43, 33.87, 82.95, 116.16, 133.03, 169.56; HRMS *m/z* 182.1298 (Calcd for $C_{11}H_{18}O_2$, 182.1307). GC examination (15 m DB 1701 glass capillary column) showed that the compound was 97% pure.

(E)-1-Trimethylsilyl-4-(1'-trimethylsilyloxy-1'-propyl)-3-methyl-3-decen-1-yne (**20g**)

Following the procedure for the preparation of **20e**, sequential treatment of (*E*)-1-trimethylsilyl-3,4-bis(trimethylstannyl)-3-decen-1-yne **4** (1.5 mmol) with methyllithium (1.5 mmol), methyl iodide (1.5 mmol) methyllithium (1.65 mmol), propanal (1.65 mmol) and chlorotrimethylsilane (1.65 mmol) yielded 0.44 g (83%) of **20g**: bp 78–81 °C (10^{-2} Torr); n^{25}D 1.4654; IR (neat) 2970, 2935, 2860, 2145, 1465, 1250, 1094, 1054, 1010, 875, 845, 763 cm^{-1}; ^{1}H NMR δ 0.09 (s, 9H, $SiMe_3$), 0.18 (s, 9H, $SiMe_3$), 0.83–0.90 (m, 6H, CH_3), 1.3–1.6 (bm, 8H, CH_2), 1.79 (s, 3H, C=CCH_3), 1.9–2.3 (m, 4H, C=CCH_2, $OCCH_2$), 4.86 (t, J = 7.0 Hz, 1H, OCH); ^{13}C NMR δ −0.02 (3 C's), 0.08 (3 C's), 10.59, 14.08, 18.34, 22.65, 27.23, 29.52, 29.66, 30.11, 31.67, 76.17, 96.40, 106.51, 113.38, 151.80; HRMS *m/z* 352.2622 (Calcd for $C_{20}H_{40}OSi_2$, 352.2618). GC examination (30 m DB 210 glass capillary column) revealed that the compound contained 2 minor impurities.

3,6-Dihydro-4-methyl-5-n-hexyl-6-ethyl-2H-pyran-2-one (**22g**)

Following the procedure for the preparation of **13a**, hydroboration of **20g** (1.5 mmol), followed by oxidation and lactonization furnished 91% of **22g**: bp 80–86°C (0.01 Torr); n^{27} D 1.4715; IR (neat) 2975, 2950, 2870, 1737, 1462, 1381, 1220, 1056, 1051 cm^{-1}; ^{1}H NMR δ 0.87 (t, J = 6 Hz, 3H, CH_3), 0.95 (t, J = 7.5 Hz, 3H, CH_3), 1.2–1.65 (bm, 8H, CH_2), 1.69 (s, 3H, C=CCH_3), 1.7–1.9 (m, 2H, C=CCH_2), 2.15–2.3 (m, 2H, OCCH2), 2.86 (d, J = 21.3 Hz, 1H, C=CCHO), 3.99 (dt, J = 21.3, 1.2 Hz, 1H, C=CCHO), 4.66 (dt, J = 3.5, 1.2 Hz, 1H, OCH); ^{13}C NMR δ 9.17, 13.97, 17.71, 22.52, 27.61, 28.39, 28.83, 29.20, 31.55, 35.50, 83.53, 122.46, 130.13, 170.66. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.94; H, 10.78. Found: C, 74.43; H, 10.63. GC examination (15 m DB 1701 glass capillary column) revealed the compound to be 99% isomerically pure.

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