Synthesis of the Pseudopterane and Furanocembrane Ring Systems by Intraannular Cyclization of β- and γ-Alkynyl Allylic Alcohols

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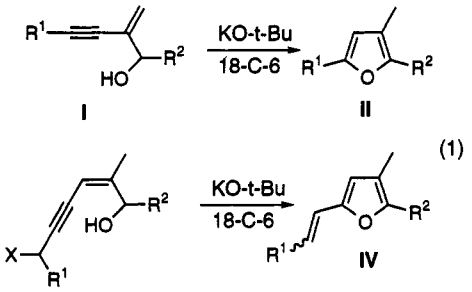
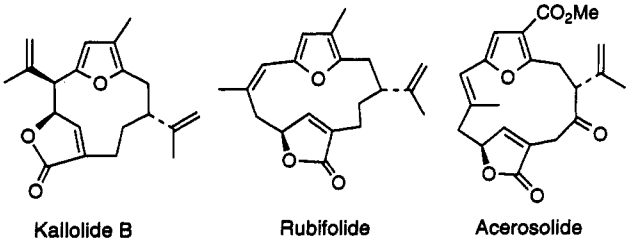
The prototype pseudopterane and furanocembrane systems **15** and **26** were prepared through a "furan last" approach. The former was obtained in 64% yield upon treatment of the 12-membered β-alkynyl allylic alcohol **14** with KO-*t*-Bu and 18-c-6 in THF–*t*-BuOH. The latter was formed in 88% yield from the 14-membered γ-alkynyl allylic alcohol **25** under comparable conditions. The carbocyclic precursors to these allylic alcohols, **11** and **24**, were secured through intramolecular Horner–Emmons condensation of keto phosphonates **10** and **23**, respectively, under Masamune–Roush conditions.

We recently described two novel approaches to furans through treatment of β- and γ-alkynyl allylic alcohols with KO-*t*-Bu and 18-crown-6 in THF–*t*-BuOH (eq 1).[1] These

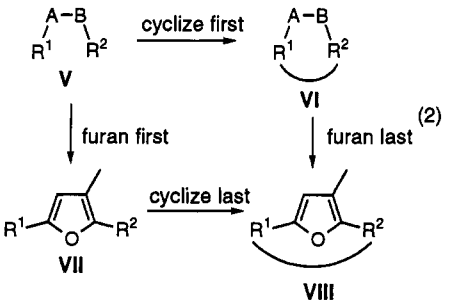


(1)

reactions proceed readily at room temperature or below and afford a variety of substituted furans in high yield. Accordingly, we felt the methodology might be applicable to the synthesis of 12- and 14-membered 2,5-furanocycles. These relatively strained ring systems are present in pseudopterane and furanocembrane natural products such as kallolide B,[2] rubifolide,[3] and acerosolide.[4,5]

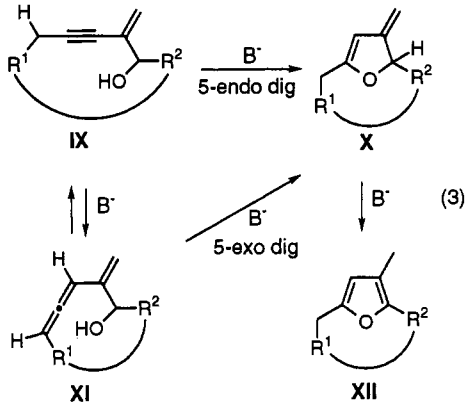


The present study was undertaken to test the feasibility of using the above cycloisomerization reactions in a "furan last" approach to these compounds (eq 2).[6] Success would depend upon the ability of the furan forming reaction to overcome the considerable ring strain associated with these bridged systems.



(2)

A Pseudopterane Prototype. Our initial efforts were directed toward the synthesis of a cyclic β-alkynyl allylic alcohol system **IX**. On the basis of our earlier findings, conversion to the 2,5-furanocycle **XII** could proceed by a direct 5-endo-*dig* and/or a 5-*exo-dig* cyclization—the latter via the vinylallene **XI** (eq 3).[1] The preference for one or



(3)

both of these pathways would depend in part on the relative ring strain of **IX** *vs* **XI**. Ultimate formation of the strained furanocycle **XII** requires deprotonation of the hydrofuran **X**. Presumably, this process would be assisted by the furan resonance stabilization.

We chose the enynol **14** as a precursor to a prototype system for kallolide B. Our starting material for this synthesis, diol **1**, was available in 74% yield from δ-vale-

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(1) Marshall, J. A.; DuBay, W. J. *J. Org. Chem.* **1993**, *58*, 3435.

(2) Look, S. A.; Burch, M. T.; Fenical, W.; Wi-tai, Z.; Clardy, J. *J. Org. Chem.* **1985**, *50*, 574.

(3) Williams, D.; Andersen, R. J.; Van Duyne, G. D.; Clardy, J. *J. Org. Chem.* **1987**, *52*, 332.

(4) Chan, W. R.; Tinto, W. F.; Laydoo, R. S.; Manchaud, P. S.; Reynolds, W. F.; McLean, S. *J. Org. Chem.* **1991**, *56*, 1773.

(5) For other approaches to these classes of natural products see: Kando, A.; Ochi, T.; Tokoroyama, T.; Siro, M. *Chem. Lett.* **1987**, 1491. Paterson, I.; Gardner, M.; Banks, B. J. *Tetrahedron Lett.* **1989**, *45*, 5283. Astley, M. P.; Pattenden, G. *Synlett.* **1991**, 335. Paquette, L. A. *Chemtracts: Org. Chem.* **1992**, *5*, 141 and references cited therein to original papers from the Paquette group.

(6) *Cf.* Marshall, J. A.; Wang, X-j. *J. Org. Chem.* **1991**, *56*, 960.

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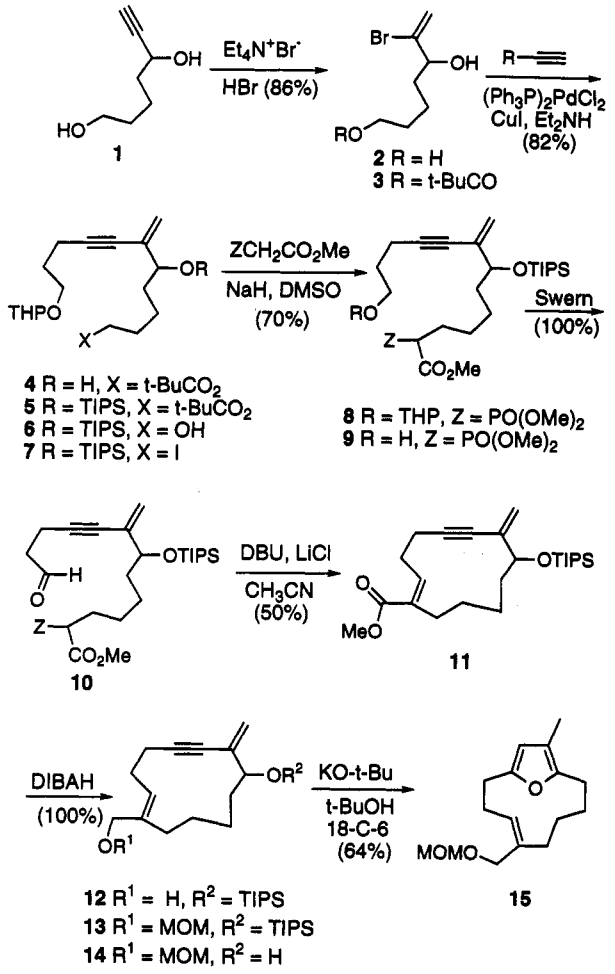
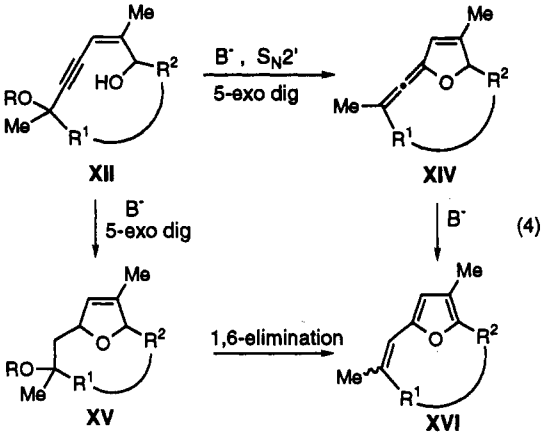
rolactone by reduction to the lactol with DIBAH and subsequent reaction with TMS acetylide. Addition of HBr



led to the vinyl bromide **2**.[7] Monoprotection as the pivalate **3** followed by Pd-promoted coupling with the THP ether of 4-pentyn-1-ol afforded the enyne **4**.[8] The derived iodide **7**[9] was converted to the phosphono ester **8** through treatment with sodium trimethylphosphonoacetate in DMSO. Selective hydrolysis of the THP group and subsequent Swern oxidation yielded the cyclization precursor, aldehyde **10**.[10] Of the several methods examined, the Masamune–Roush procedure was the most satisfactory for the cyclization of **10** affording the 12-membered unsaturated ester **11** in 50% yield.[11] The stereochemistry of the conjugated double bond is assigned from chemical shift and coupling constant data for the vinylic proton and by analogy to closely related cyclizations.[12]

In view of the strongly basic conditions required for the furan reaction, we elected to reduce ester **11** to the alcohol **12**, which was protected as the MOM ether **13**. The derived enynol **14** readily cyclized upon exposure to KO-*t*-Bu and 18-c-6 in THF–*t*-BuOH at room temperature, affording the 12-membered 2,5-furanocycle **15** in 64% yield.

Furanocembrane Ring System. In our next application of the "furan last" approach to 2,5-furanocycles, we wished to employ our S_N2' methodology (eq 1) to synthesize a vinylfuran prototype of the furanocembranes. This reaction could proceed by a direct 5-*exo*-*dig*/S_N2' cyclization followed by [1,5] isomerization or by stepwise 5-*exo*-*dig* cyclization and subsequent 1,6-elimination as illustrated in eq 4. We felt that this particular furan-forming



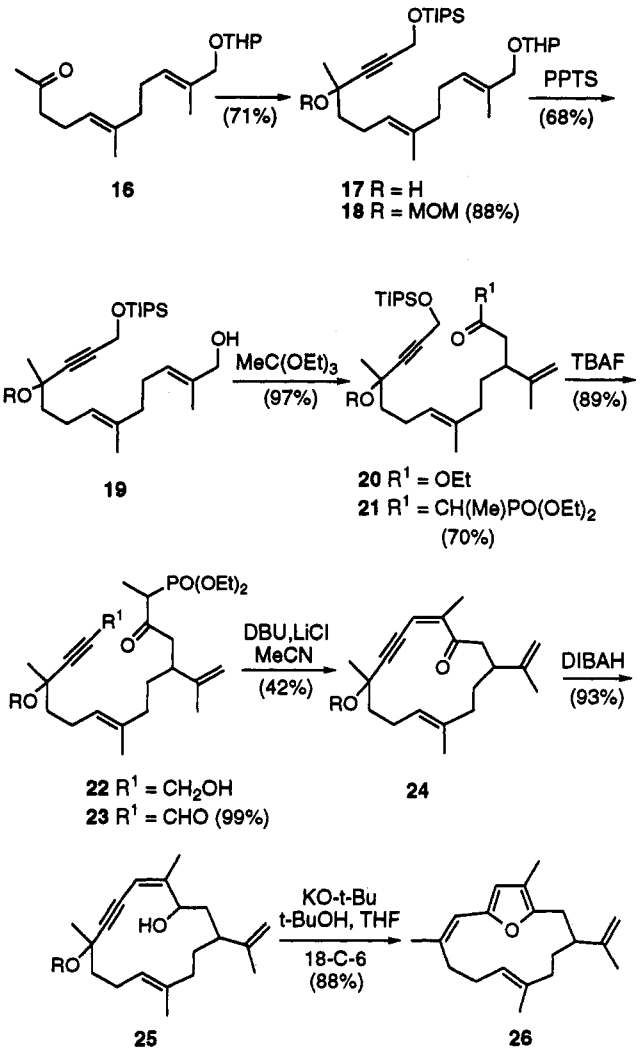
(4)

reaction would be especially well suited to strained furanocycles because of its exothermicity in acyclic systems.[1] However, there was some uncertainty with regard to double bond stereochemistry. Molecular mechanics calculations indicate that in rubifolide and related systems the (*Z*) double bond isomer is preferred by some 5–7 kcal over the (*E*) isomer.[13] Thus, it might be possible to obtain the former through equilibration, if the latter was kinetically favored. The (*Z*) isomer is related to rubifolide and the (*E*) isomer to acerosolide.

Our synthesis of the rubifolide prototype **26** began with ketone **16**, obtained from geranylacetone by selective allylic oxidation with SeO_2–*t*-BuOOH followed by protection of the resulting allylic alcohol as the THP ether.[14] Addition of the lithio derivative of TIPS-protected propargyl alcohol gave the expected tertiary alcohol **17** in 71% yield. The MOM derivative **18** was converted to alcohol **19** with PPTS in MeOH. Homologation by orthoester Claisen rearrangement gave the ester **20**, a 1:1 mixture of diastereomers, in 97% yield.[15] Addition of lithium diethyl ethylphosphonate led to phosphono ketone **21** in 70% yield.[16]

The cyclization substrate, aldehyde **23**, was secured upon TIPS removal with TBAF–HOAc and subsequent Swern oxidation.[10] Application of the Masamune–Roush procedure afforded the enone **24** in 42% yield.[11] For this model system we did not examine the foregoing cyclization in any detail, nor did we attempt to establish the enone stereochemistry. The indicated (*Z*) isomer is *ca.* 1.5 kcal lower in energy than the (*E*) isomer according to calculation.[13] However, we have previously shown that both (*Z*)

(7) Cousseau, J. *Synthesis* **1980**, 805.
(8) Sonogashiro, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.
(9) Lange, G. L.; Gottardo, C. *Synth. Commun.* **1990**, *20*, 1473.
(10) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.
(11) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, 2183.
(12) Marshall, J. A.; DeHoff, B. S. *Tetrahedron* **1987**, *43*, 4860. *E.g.*, δ 5.90 ppm (J = 6.5 Hz) for a related 14-membered system *vs* δ 5.92 ppm (J = 6.7 Hz) for **11**.
(13) The program Macromodel V3.5 was employed for these calculations. Global minimum multiple conformer searching was achieved with the Monte Carlo subroutine in BATCHMIN through multistep iterations (300–1000) until the minimum energy conformer was found multiple times (10 or more). For a description of the program, see: Mohamadi, F.; Richards, N. G. J.: Guida, W. C.; Liskamp, R.; Lipton, M.; Caulfield, C.; Chang, G.; Henrickson, T.; Still, W. C., *J. Comput. Chem.* **1990**, *11*, 440. Chang, G.; Guida, W. C.; Still, W. C., *J. Am. Chem. Soc.* **1989**, *111*, 4379.
(14) McMurray, J. E.; Dushin, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 6942.
(15) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T. *J. Am. Chem. Soc.* **1970**, *92*, 741.
(16) Boger, D. L.; Curran, T. T. *J. Org. Chem.* **1992**, *57*, 2235.



and (*E*) acyclic allylic alcohol analogues of **25** are converted to vinylfurans with base.[1] The latter reaction most likely involves prior isomerization to a vinylallene or cumulene. In any event, reduction of enone **24** with DIBAH and subsequent base treatment afforded the furanocycle **26** in 88% yield as a single isomer according to the ^1H and ^{13}C NMR spectra. The double-bond stereochemistry was established by a NOESY experiment. We were unable to detect any of the (*E*) isomer of **26** in this reaction. Molecular mechanics calculations reveal significant twisting of the vinylfuran double bond in the (*E*) isomer.[13] The (*Z*) double bond in **26**, on the other hand, is untwisted and coplanar with the furan ring. These calculations suggest that the synthesis of (*E*) vinyl furanocycles will require methodology that precludes double bond equilibration.[17]

The present studies demonstrate the applicability of alkynyl allylic alcohols in our "furan last" approach to pseudopteranes and certain furanocembranes. Future work will address the problem of butenolide incorporation in these systems.

Experimental Section[18]

1-Heptyne-3,7-diol (1). To a solution of 25.0 g (0.25 mol) of (trimethylsilyl)acetylene in 250 mL of THF was added 102 mL (0.25 mol) of 2.5 M *n*-BuLi in hexanes at −78 °C. To a solution of 23.6 mL (0.25 mol) of δ-valerolactone in 250 mL of THF in a separate flask was added 170 mL of 1.5 M DIBALH in toluene at −78 °C. Both reactions were stirred for 45 min, and then the lactol solution was cannulated into the (trimethylsilyl)acetylide solution. After the addition, the reaction mixture was warmed to rt and stirred for 12 h. The reaction mixture was quenched with 250 mL of MeOH at 0 °C and concentrated under reduced pressure. Water was added, the layers were separated, and the ether layer was dried over $MgSO_4$ and concentrated under reduced pressure. Bulb-to-bulb distillation (120 °C, 0.5 Torr) afforded 24.1 g (74%) of diol **1** as a clear and colorless oil: IR (film, cm^{-1}) 3363, 3287, 2111; ^1H NMR (300 MHz, $CDCl_3$) δ 4.37 (m), 3.66 (m), 2.45 (d, J = 2.1 Hz), 1.87 (d, J = 5.4 Hz), 1.78–1.54 (m), 1.30 (m); ^{13}C NMR (125 MHz, $CDCl_3$) 85.4, 73.2, 62.7, 62.2, 37.5, 32.3, 21.6; HRMS calcd for $C_7H_{13}O_2$ ($M^+ + H$) 129.0916, found 129.0918.

2-Bromo-1-heptene-3,7-diol (2). The method of Cousseau was employed.[7] Gaseous HBr (15.2 g, 0.19 mol) was added as a slow stream into a dispersion of 26.2 g (0.12 mol) of dry Et_4NBr in 125 mL of CH_2Cl_2 with stirring and cooling in ice. A solution of 16.0 g (120 mmol) of alkyne **1** in 10 mL of CH_2Cl_2 was then added, and the flask was stoppered at rt for 3 h. The reaction mixture was cooled to 0 °C and diluted with 125 mL of ether and 25 mL of Et_3N. The Et_4NBr was removed by filtration, and the filtrate was concentrated under reduced pressure. Purification by filtration through silica gel (50% EtOAc–hexane) afforded 22.4 g (86%) of vinyl bromide **2** as a clear, yellow oil. IR (cm^{-1}, film) 3335, 1627; ^1H NMR (500 MHz, $CDCl_3$) δ 5.86 (dd 1 H, J = 0.7, 1.9 Hz), 5.54 (d, J = 1.9 Hz), 4.10 (dd, J = 6.7, 7.0 Hz), 3.65 (t, J = 6.4 Hz), 1.73–1.38 (m). ^{13}C NMR (125 MHz, $CDCl_3$) 137.7, 117.1, 76.0, 62.6, 35.1, 32.4, 21.8.

6-Bromo-5-hydroxy-6-heptenyl Pivalate (3). To a solution of 13.0 g (62.2 mmol) of diol **2** in 120 mL of 1:1 pyridine/CH_2Cl_2 at 0 °C was added 7.70 g (62.2 mmol) of $(CH_3)_3CCOCl$ all at once. After 20 min, the reaction mixture was quenched with water, and diluted with ether, and the layers were separated. The organic layer was washed with 10% HCl, saturated aqueous $CuSO_4$, and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by filtration through silica gel (10% EtOAc–hexane) afforded 13.0 g (74%) of pivaloyl ester **3**: IR (cm^{-1}, film) 3440, 1726, 1163; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86, 5.55 (s), 4.03–4.10 (m), 4.05 (t, J = 6.5 Hz), 1.39–1.73 (m), 1.18 (s); ^{13}C NMR (75 MHz, $CDCl_3$) 178.8, 137.3, 116.9, 75.7, 64.1, 38.7, 34.7, 28.3, 27.2, 21.6; HRMS calcd for $C_{12}H_{21}O_3Br$ ($M^+ + H$) 293.0737, found 293.0737.

5-Hydroxy-6-methylene-11-(tetrahydropyranyloxy)-7-undecynyl Pivalate (4). The method of Sonogashiro was employed.[8] To a solution of 11.3 g (40.2 mmol) of vinyl bromide **3** in 270 mL of diethylamine was added 1.41 g (2.00 mmol) of bis(triphenylphosphine)palladium(II) chloride and 765 mg (4.02 mmol) of copper iodide to yield a dark green solution. A solution of 7.44 g (44.2 mmol) of 5-(tetrahydropyranyloxy)-1-pentyne in 5 mL of diethylamine was added to the reaction mixture at rt. The solution turned yellow within 15 min. The reaction mixture was stirred at rt for 2 h, and then it was diluted with ether and quenched with saturated aqueous NH_4Cl. The mixture was separated, and the organic layer was washed with saturated aqueous NH_4Cl and brine and dried over $MgSO_4$. Purification by flash chromatograhy on silica gel (25% EtOAc–hexane) afforded 12.5 g (82%) of enyne **4**: IR (cm^{-1}, film) 3442, 2222, 1727, 1160; ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (d, J = 5.1 Hz), 4.57–4.58 (m), 4.02–4.06 (m), 3.80–3.91 (m), 3.45–3.56 (m), 2.44 (t, J = 7.1 Hz), 1.35–1.84 (m); ^{13}C NMR (75 MHz, $CDCl_3$) 178.6, 135.1, 119.4, 98.7, 91.9, 78.2, 74.4, 65.8, 64.2, 62.1, 38.7, 35.4, 30.6, 28.8, 28.4, 27.1, 25.4, 21.8, 19.4, 16.2; HRMS calcd for $C_{22}H_{36}O_5$ (M^+) 380.2569, found 380.2563. Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H; 9.54. Found: C, 69.19; H, 9.52.

6-Methylene-11-(tetrahydropyranyloxy)-5-[(triisopropylsilyl)oxy]-7-undecynyl Pivalate (5). To a solution of 12.5 g (32.9 mmol) of alcohol **4** and 5.74 mL (49.3 mmol) of 2,6-lutidine in 130 mL of CH_2Cl_2 was added 8.83 mL (32.9 mmol) of triisopropylsilyl triflate at rt. After 45 min, the reaction mixture was diluted with ether and water, and the layers were separated.

(17) *Cf.* Astley, M. P.; Pattenden, G. *Synthesis* **1992**, 101. These authors describe a "furan last" approach to the (*E*)-isomer of vinylfuran **26** through acid-catalyzed intraannular cyclization of a 1,4-diketone precursor. The ^1H NMR spectrum of their material was quite similar to that of our furan **26**, but an exact matchup was not possible because of differing spectrometer field strengths.

(18) For typical experimental protocols see: Marshall, J. A., Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *56*, 647.

The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 15.3 g (87%) of silyl ether **5**: IR (film, cm^{-1}) 2223, 1730, 1614, 1157; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40 (s), 5.33 (s), 4.56–4.58 (m), 4.23–4.26 (m), 4.02 (t, J = 6.6 Hz), 3.79–3.85 (m), 3.43–3.48 (m), 2.41 (t, J = 7.0 Hz), 1.23–1.83 (m), 1.17 (s), 1.04 (s); ^{13}C NMR (75 MHz, $CDCl_3$) 178.4, 134.9, 119.2, 98.7, 90.9, 79.2, 74.7, 65.8, 64.3, 62.0, 38.6, 35.9, 30.6, 28.9, 28.7, 27.1, 25.5, 20.2, 19.4, 18.0, 16.2, 12.3; HRMS calcd for $C_{31}H_{56}O_5Si$ (M^+) 536.3897, found 536.3899. Anal. Calcd for $C_{31}H_{56}O_5Si$: C, 69.35; H; 10.52. Found: C, 69.39; H, 10.51.

6-Methylene-11-(tetrahydropyranyloxy)-5-[(triisopropylsilyl)oxy]-7-undecyn-1-ol (6). To a solution of 13.6 g (25.3 mmol) of pivaloyl ester **5** in 100 mL of Et_2O at −78 °C was added 35.5 mL (53.2 mmol) of a 1.5 M solution of DIBAH in toluene. The mixture was stirred for 30 min, quenched with water, and warmed to rt, and the layers were separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (25% EtOAc–hexane) afforded 10.7 g (93%) of allylic alcohol **6**: IR (film, cm^{-1}) 3423, 2224, 1614, 1119; ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (s), 5.33 (s), 4.58–4.60 (m), 4.24–4.26 (m), 3.78–3.85 (m), 3.61 (t, J = 6.6 Hz), 3.43–3.50 (m), 2.42 (t, J = 7.0 Hz), 1.24–1.85 (m), 1.04 (s). ^{13}C NMR (75 MHz, $CDCl_3$) 135.0, 119.4, 98.7, 90.8, 79.4, 74.8, 65.9, 62.7, 62.0, 36.2, 32.8, 30.6, 28.8, 25.4, 20.0, 19.4, 18.1, 16.2, 12.4; HRMS calcd for $C_{26}H_{48}O_4Si$ (M^+) 452.3322, found 452.3322. Anal. Calcd for $C_{26}H_{48}O_4Si$: C, 68.97; H; 10.69. Found: C, 68.82; H, 10.74.

11-Iodo-6-methylene-1-(tetrahydropyranyloxy)-7-[(triisopropylsilyl)oxy]-4-undecyne (7). The method of Lange was employed.[9] To 35 mL of CH_2Cl_2 were added, in order, 2.56 g (10.1 mmol) of triphenylphosphine, 0.686 g (10.1 mmol) of imidazole, and after the imidazole was completely dissolved, 2.64 g (10.1 mmol) of iodine. A solution of 3.80 g (8.39 mmol) of alcohol **6** in 5 mL of CH_2Cl_2 was added, and the mixture was stirred at rt for 45 min. The reaction mixture was then concentrated under reduced pressure, diluted with ether, filtered through silica gel, and concentrated under reduced pressure to afford 4.58 g (97%) of iodide **7**: IR (film, cm^{-1}) 2224, 1614, 1035; ^1H NMR (500 MHz, $CDCl_3$) δ 5.42 (s), 5.34 (s), 4.56–4.58 (m), 4.23–4.26 (m), 3.79–3.85 (m), 3.43–3.48 (m), 3.15 (t, J = 7.2 Hz), 2.41 (dt, J = 2.1, 7.2 Hz), 1.36–1.83 (m) 1.04 (s); ^{13}C NMR (75 MHz, $CDCl_3$) 135.2, 119.8, 98.1, 91.4, 79.6, 75.0, 66.3, 62.5, 35.6, 34.2, 31.1, 29.3, 25.9, 25.3, 19.9, 18.5, 16.7, 12.8, 7.1; HRMS calcd for $C_{23}H_{40}O_3ISi$ (M^+ − *i*-Pr) 519.1792, found 519.1788. Anal. Calcd for $C_{26}H_{47}O_3ISi$: C, 55.50; H, 8.42; I, 22.55. Found: C, 55.28; H, 8.39; I, 22.75.

Methyl 13-(Tetrahydropyranyloxy)-2-(dimethylphosphono)-8-methylene-7-[(triisopropylsilyl)oxy]-9-tridecynoate (8). To a slurry of 200 mg (7.96 mmol) of 95% NaH in 6 mL of DMSO at rt was added 1.15 mL (7.11 mmol) of trimethyl α-phosphonoacetate dropwise. The resulting solution was stirred for 30 min and then treated with 3.20 g (5.69 mmol) of iodide **7**. After being stirred for 12 h, the reaction mixture was diluted with ether and quenched with water, and the layers were separated. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (80% EtOAc–hexane) afforded 2.46 g (70%) of phosphonate **8**: IR (film, cm^{-1}) 2222, 1739, 1034; ^1H NMR (500 MHz, $CDCl_3$) δ 5.38 (s, vinyl H), 5.31 (s), 4.56–4.58 (m), 4.19–4.22 (m), 3.73–3.84 (m), 3.43–3.49 (m), 2.96 (ddd, J = 22.6, 11.2, 3.7 Hz), 2.40 (dt, J = 2.7, 7.2 Hz), 1.22–2.00 (m), 1.03 (s). HRMS calcd for $C_{28}H_{50}O_8PSi$ (M^+ CH(CH_3)$_2$) 573.3013, found 573.3019. Anal. Calcd for $C_{31}H_{57}O_8PSi$: C, 60.36; H; 9.32. Found: C, 60.46; H, 9.36.

Methyl 2-(Dimethylphosphono)-13-hydroxy-8-methylene-7-[(triisopropylsilyl)oxy]-9-tridecynoate (9). To a solution of 2.00 g (3.24 mmol) of THP ether **8** in 35 mL of MeOH was added 81.0 mg (0.320 mmol) of PPTS at rt. The reaction mixture was allowed to stir for 24 h, and then it was concentrated under reduced pressure. The concentrate was diluted with ether and water, and the layers were separated. The aqueous layer was extracted with ethyl acetate, and the extracts were combined, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc) afforded 1.52 g (88%) of alcohol **9**: IR (film, cm^{-1}) 3468, 2224, 1739, 1034; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40–5.42 (m), 5.32 (s), 4.19–4.24 (m), 3.74–3.79 (m), 2.96 (dddd, J = 22.8, 10.9, 4.1, 3.1 Hz), 2.42 (t, J = 6.8 Hz), 2.38 (bs), 1.19–2.00 (m), 1.03 (s); ^{13}C NMR (75 MHz, $CDCl_3$) 169.5, 134.8, 119.2, 91.0, 79.2, 74.7, 61.2, 53.4, 52.5, 45.8, 44.1, 35.9, 31.3, 28.4, 26.8, 23.2, 18.0, 15.9, 12.3; HRMS calcd for $C_{26}H_{49}O_7PSi$ (M^+) 532.2985, found 532.2983. Anal. Calcd for $C_{26}H_{49}O_7PSi$: C, 58.62; H; 9.27. Found: C, 58.72; H, 9.34.

Methyl 2-(Dimethylphosphono)-12-formyl-8-methylene-7-[(triisopropylsilyl)oxy]-9-dodecynoate (10). The method of Swern was employed.[10] To a solution of 0.42 mL (4.79 mmol) of oxalyl chloride in 15 mL of CH_2Cl_2 was added 0.45 mL (6.38 mmol) of DMSO at −78 °C. The mixture was stirred for 15 min, and then 1.70 g (3.19 mmol) of alcohol **9** in 15 mL of CH_2Cl_2 was added slowly. After an additional 15 min, 1.78 mL (12.8 mmol) of triethylamine was added, and the reaction mixture was stirred for 5 min, and then allowed to warm to rt. The reaction mixture was then diluted with ether, and quenched with water, and the layers were separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure to yield 1.69 g (100%) of aldehyde **10** as a clear yellow oil: IR (film, cm^{-1}) 2724, 2226, 1739, 1732, 1032; ^1H NMR (300 MHz, $CDCl_3$) δ 9.78 (s), 5.40 (s), 5.33 (s), 4.19–4.24 (m), 3.74–3.79 (m), 2.98 (dddd, J = 22.7, 10.9, 3.9, 1.1 Hz), 2.60–2.72 (m), 1.19–2.00 (m), 1.03 (s).

(*Z*)-1-Carbomethoxy-7-methylene-8-[(triisopropylsilyl)oxy]-1-cyclododecen-5-yne (11). The method of Masamune and Roush was employed.[11] To a stirred suspension of 367 mg (8.67 mmol) of LiCl and 648 μL (4.33 mmol) of DBU in 90 mL of acetonitrile was added 460 mg (0.867 mmol) of phosphonate **10** in 20 mL of CH_3CN over 4 h. The reaction mixture was allowed to stir for an additional 2 h, and then it was concentrated under reduced pressure, diluted with ether and water, and the layers separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 175 mg (50%) of enyne **11**: IR (film, cm^{-1}) 2224, 1716, 1644, 1613, 1108; ^1H NMR (300 MHz, $CDCl_3$) δ 5.92 (t, J = 6.7 Hz), 5.43–5.45 (m), 5.31–5.32 (m), 4.28–4.30 (m), 3.71 (s), 2.65–2.85 (m), 2.44–2.49 (m), 2.35 (bs), 1.09–1.88 (m), 1.03 (s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 143.1, 134.4, 130.9, 119.4, 90.8, 81.7, 74.4, 51.1, 34.7, 33.5, 27.7, 25.5, 19.4, 19.1, 18.1, 12.4; HRMS calcd for $C_{24}H_{40}O_3Si$ (M^+) 404.2747, found 404.2751.

(*Z*)-9-(Hydroxymethyl)-3-methylene-4-[(triisopropylsilyl)oxy]-9-cyclododecen-1-yne (12). The procedure described for alcohol **6** was employed with 170 mg (0.420 mmol) of ester **11** in 2 mL of Et_2O and 620 μL (0.920 mmol) of a 1.5 M solution of DIBAH in toluene. Purification of the product by flash chromatography on silica gel (50% EtOAc–hexane) afforded 160 mg (100%) of allylic alcohol **12**: IR (film, cm^{-1}) 3332, 2224, 1614, 1108; ^1H NMR (500 MHz, $CDCl_3$) δ 5.44–5.46 (m), 5.29–5.30 (m), 4.29–4.30 (m), 4.09, 4.16 (AB, J = 11.8 Hz), 2.22–2.45 (m), 1.17–1.87 (m), 1.03 (s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 134.4, 129.9, 119.2, 91.0, 82.0, 74.4, 59.2, 34.3, 33.7, 26.1, 24.2, 20.1, 19.3, 18.1, 12.4; HRMS calcd for $C_{23}H_{40}O_2Si$ (M^+) 376.2798, found 376.2797. Anal. Calcd for $C_{23}H_{40}O_2Si$: C, 73.34; H, 10.71. Found: C, 73.20; H, 10.78.

(*Z*)-9-[(Methoxymethoxy)methyl]-3-methylene-4-[(triisopropylsilyl)oxy]-9-cyclododecen-1-yne (13). To a solution of 145 mg (0.380 mmol) of alcohol **12** and 200 μL (1.15 mmol) of diisopropylethylamine in 2 mL of CH_2Cl_2 at 0 °C was added 44.0 μL (0.580 mmol) of MOMCl. The reaction mixture was allowed to stir for 6 h, and then it was diluted with ether and water and the layers were separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 155 mg (97%) of methoxymethoxy ether **13**: IR (film, cm^{-1}) 2225, 1614, 1047; ^1H NMR (500 MHz, $CDCl_3$) δ 5.43 (s), 5.36–5.38 (m), 5.28 (s, vinyl H), 4.59 (s), 4.29–4.30 (m), 4.01, 4.09 (AB, J = 11.3 Hz), 3.35 (s), 2.22–2.45 (m), 1.17–1.87 (m), 1.03 (s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.9, 134.5, 131.1, 119.0, 95.5, 90.9, 81.8, 74.5, 63.1, 55.2, 34.2, 33.7,

26.2, 24.1, 20.0, 19.3, 18.1, 12.4; HRMS calcd for $C_{25}H_{44}O_3Si$ (M^+) 420.3060, found 420.3060.

(*Z*)-8-[(Methoxymethoxy)methyl]-2-methylene-7-cyclododecen-3-yn-1-ol (14). To a solution of 150 mg (0.360 mmol) of silyl ether **13** in 2 mL of THF was added 1.07 mL (1.07 mmol) of 1.0 M TBAF in THF at 0 °C. The reaction mixture was stirred for 3 h at rt, and then it was diluted with ether and water and the layers were separated. The organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (25% EtOAc–hexane) afforded 83.0 mg (88%) of alcohol **14**: IR (film, cm^{-1}) 3444, 2224, 1616, 1039; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40–5.42 (m), 5.35 (s, vinyl H), 5.30 (s), 4.59 (s), 4.04–4.08 (m), 4.12, 4.00 (AB, J = 11.3 Hz), 3.36 (s), 2.22–2.46 (m), 1.45–1.84 (m), 1.18–1.26 (m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 134.6, 131.1, 120.5, 95.5, 91.9, 80.2, 75.6, 63.0, 55.3, 33.8, 33.1, 26.1, 23.9, 21.5, 19.2. HRMS calcd for $C_{16}H_{24}O_3$ (M^+) 264.1725, found 264.1715. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.57; H, 9.10.

Furan 15. To a solution of 220 mg (0.850 mmol) of 18-crown-6, 850 μL (0.850 mmol) of 1.0 M potassium *tert*-butoxide in THF, and 80.0 μL (0.850 mmol) of *tert*-butyl alcohol was added 45.0 mg (0.17 mmol) of alcohol **14** in 1 mL of THF. After being stirred for 10 h, the reaction mixture was diluted with ether and quenched with 10% aqueous K_2CO_3. The aqueous layer was extracted with ether, and the combined organic extracts were washed with 10% aqueous K_2CO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (5% EtOAc–hexane) afforded 29.0 mg (64%) of furan **15**: δ ^1H NMR (300 MHz, $CDCl_3$) δ 5.71 (s), 5.47 (t, J = 8.4 Hz), 4.45 (s), 4.52 (bs), 3.30 (s, OCH_3), 2.65 (t, J = 6.4 Hz), 2.39 (dd, J = 5.8, 6.1 Hz), 2.27–2.36 (m), 1.97 (dd, J = 5.3, 5.5 Hz), 1.84 (s), 1.76–1.86 (m), 1.27–1.37 (m); ^{13}C NMR (75MHz, $CDCl_3$) 153.3, 148.4, 135.9, 129.5, 116.0, 108.4, 95.0, 62.1, 55.2, 36.6, 29.1, 27.4, 26.8, 26.5, 24.1, 9.8. HRMS calcd for $C_{16}H_{24}O_3$ (M^+) 264.1725, found 264.1734. Anal. Calcd for $C_{16}H_{24}O_3$: C; 72.69, H; 9.15. Found: C; 72.72, H; 9.14.

(5*E*,9*E*)-6,10-Dimethyl-11-(tetrahydropyranyloxy)-5,9-undecadien-2-one (16). To a solution of 1.80 g (8.56 mmol) of (5*E*,9*E*)-6,10-dimethyl-11-hydroxy-5,9-undecadien-2-one[14] in 35 mL of CH_2Cl_2 was added 0.94 mL (10 mmol) of dihydropyran and 0.22 g (0.86 mmol) of PPTS. The reaction mixture was stirred for 10 h, and then it was quenched with water and ether and the layers were separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 2.44 g (97%) of THP ether **16**: IR (cm^{-1}, film) 1717, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 5.37 (t, J = 6.9 Hz), 5.05 (t, J = 7.1 Hz), 4.57 (dd, J = 2.9, 3.9 Hz), 4.07, 3.81 (AB, J = 11.3 Hz), 3.80–3.88 (m), 3.46-3.50 (m), 2.44 (t, J = 7.5 Hz), 2.01–2.27 (m), 2.11 (s), 1.51–1.96 (m), 1.63 (s), 1.59 (s); ^{13}C NMR (75 MHz, $CDCl_3$) 208.4, 135.8, 131.9, 127.5, 122.8, 97.2, 72.7, 62.0, 43.5, 39.1, 30.6, 29.8, 26.1, 25.4, 22.3, 19.4, 15.8, 13.9; HRMS calcd for $C_{18}H_{30}O_3$ (M^+) 294.2195, found 294.2191.

(7*E*,11*E*)-13-(Tetrahydropyranyloxy)-1-[(triisopropylsilyl)oxy]-4,8,12-trimethyl-7,11-tridecadien-2-yn-4-ol (17). To a solution of 4.33 g (20.4 mmol) of 3-[(triisopropylsilyl)oxy]-1-propyne in 65 mL of THF at 0 °C was added 8.20 mL (20.4 mmol) of a 2.5 M solution of *n*-BuLi in hexanes. After 15 min, the reaction mixture was cooled to −78 °C, and a solution of 4.80 g (16.3 mmol) of THP ether **16** in 5 mL of THF was added all at once. Following the addition, the reaction mixture was allowed to warm to 0 °C. After an additional 2 h, the reaction mixture was diluted with ether and quenched with water, and the layers were separated. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 5.90 g (71%) of alcohol **17**: IR (cm^{-1}, film) 3429, 1101, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 5.39 (t, J = 6.9 Hz), 5.15 (t, J = 6.8 Hz), 4.58 (dd, J = 3.5, 3.8 Hz), 4.40 (s), 4.08, 3.82 (AB, J = 11.8 Hz), 3.84–3.89 (m), 3.46–3.51 (m), 1.98–2.31 (m), 1.50-1.89 (m), 1.64 (s), 1.62 (s), 1.45 (s), 1.05–1.15 (m); ^{13}C NMR (75 MHz, $CDCl_3$) 135.9, 132.3, 128.1, 124.4, 97.7, 88.4, 82.5, 73.3, 68.6, 62.4, 52.3, 43.7, 39.6, 31.0, 30.2, 26.6, 25.9, 23.9, 19.9, 18.3, 16.4, 14.4, 12.4. Anal. Calcd for $C_{30}H_{54}O_4Si$: C, 71.09; H, 10.74. Found: C, 71.17; H, 10.80.

(7*E*,11*E*)-4-(Methoxymethoxy)-13-(tetrahydropyranyloxy)-1-[(triisopropylsilyl)oxy]-4,8,12-trimethyl-7,11-tridecadien-2-yne (18). The procedure described for **13** was employed with 5.50 g (10.9 mmol) of alcohol **17** and 5.50 mL (32.6 mmol) of diisopropylethylamine in 45 mL of CH_2Cl_2 at 0 °C to which was added 1.24 mL (16.3 mmol) of MOMCl. Purification of the product by flash chromatography on silica gel (10% EtOAc–hexane) afforded 5.26 g (88%) of methoxymethoxy ether **18**: IR (cm^{-1}, film) 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 5.39 (t, J = 7.0 Hz), 5.10 (t, J = 7.1 Hz), 4.96, 4.77 (AB, J = 6.9 Hz), 4.58 (dd, J = 3.4, 4.0 Hz), 4.41 (s), 4.07, 3.82 (AB, J = 11.9 Hz), 3.84–3.89 (m), 3.46–3.52 (m), 3.36 (s), 1.97–2.21 (m), 1.47–1.86 (m), 1.64 (s), 1.59 (s), 1.45 (s), 1.02–1.18 (m); ^{13}C NMR (125 MHz, $CDCl_3$) 135.4, 132.2, 128.2, 124.4, 97.7, 93.4, 85.6, 85.1, 74.4, 73.3, 62.4, 55.8, 52.3, 43.0, 39.6, 31.0, 28.2, 26.7, 25.9, 23.5, 19.9, 18.3, 16.3, 14.4, 12.4. Anal. Calcd for $C_{32}H_{58}O_5Si$: C, 69.77; H, 10.61. Found: C, 69.84; H, 10.66.

(2*E*,6*E*)-10-Methoxymethoxy-13-(triisopropylsilyl)oxy-2,6,10-trimethyl-2,6-tridecadien-11-yn-1-ol (19). The procedure described for alcohol **9** was employed with 3.80 g (6.90 mmol) of THP ether **18** in 30 mL of MeOH and 0.17 g (0.69 mmol) of PPTS at rt. The product was purified by flash chromatography on silica gel (25% EtOAc–hexane) affording 2.00 g (62%) of alcohol **19**: IR (cm^{-1}, film) 3426, 1100, 1036; ^1H NMR (300 MHz, $CDCl_3$) δ 5.37 (t, J = 7.0 Hz), 5.11 (t, J = 7.1 Hz), 4.95, 4.78 (AB, J = 6.9 Hz), 4.41 (s), 3.97 (s), 3.36 (s), 1.97–2.21 (m), 1.62-1.80 (m), 1.65 (s), 1.60 (s), 1.48 (s), 1.46 (s), 1.02–1.18 (m); ^{13}C NMR (125 MHz, $CDCl_3$) 135.0, 134.8, 126.0, 124.1, 93.0, 85.2, 84.7, 74.1, 68.9, 55.5, 51.9, 42.6, 39.2, 27.8, 26.2, 23.1, 17.9, 15.9, 13.7, 12.0. Anal. Calcd for $C_{27}H_{50}O_4Si$: C, 69.47; H, 10.80. Found: C, 69.46; H, 10.82.

(6*E*)-Ethyl 6,10-Dimethyl-10-(methoxymethoxy)-3-isopropenyl-13-[(triisopropylsilyl)oxy]-6-tridecen-11-ynoate (20). The method of Johnson was employed.[14] A mixture of 1.75 g (3.45 mmol) of alcohol **19**, 4.40 mL (24.2 mmol) of trimethyl orthoacetate, and 16 μL (0.21 mmol) of propionic acid was heated to 140 °C for 1 h. The reaction mixture was then cooled to rt. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 1.80 g (97%) of ester **20**: IR (cm^{-1}, film) 1738, 1646, 1099, 1036; ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (t, J = 7.3 Hz), 4.96, 4.77 (AB, J = 6.9 Hz), 4.76, 4.71 (s), 4.41 (s), 4.08 (q, J = 7.1 Hz), 3.36 (s), 2.47–2.58 (m), 2.33 (d, J = 7.6 Hz), 1.84–2.20 (m), 1.37–1.75 (m), 1.64 (s), 1.57 (s), 1.45 (s), 1.22 (t, J = 7.1 Hz), 1.02–1.18 (m); ^{13}C NMR (125 MHz, $CDCl_3$) 172.6, 146.0, 135.0, 124.0, 112.2, 93.0, 85.1, 84.7, 74.0, 60.1, 55.5, 51.9, 43.3, 42.6, 39.3, 37.0, 31.2, 27.8, 23.1, 18.6, 17.9, 15.9, 14.2, 12.0. Anal. Calcd for $C_{31}H_{56}O_5Si$: C, 69.35; H, 10.52. Found: C, 69.09; H, 10.46.

(8*E*)-8,12-Dimethyl-2-(diethylphosphono)-12-(methoxymethoxy)-5-isopropenyl-15-[(triisopropylsilyl)oxy]-8-pentadecen-13-yn-3-one (21). The method of Boger was employed.[16] To a solution of 1.14 g (6.85 mmol) of ethyl diethylphosphonate[19] in 15 mL of THF at −78 °C was added 2.61 mL (6.52 mmol) of 2.5 M *n*-BuLi in hexanes. After 15 min, 1.75 g (3.26 mmol) of ester **20** was added at −78 °C. The reaction mixture was stirred for 15 min, and then it was warmed to 0 °C. After an additional 15 min, the reaction mixture was diluted with ether and quenched with aqueous NH_4Cl, and the layers were separated. The aqueous layer was washed with ether, and the combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (50% EtOAc–hexane) afforded 1.50 g (70%) of phosphono ketone **21**: IR (cm^{-1}, film) 1716, 1646, 1100, 1031; ^1H NMR (300 MHz, $CDCl_3$) δ 5.04–5.11 (m), 4.96, 4.77 (AB, J = 6.9 Hz), 4.73, 4.70 (s), 4.41 (s), 4.04–4.16 (m), 3.36 (s), 3.22 (dq, J = 25.4, 7.1 Hz), 3.17 (dq, J = 25.3, 7.1 Hz), 2.40-2.84 (m), 1.83–2.19 (m), 1.65 (s), 1.57 (s), 1.45 (s), 1.25–1.34 (m), 1.02–1.18 (m). Anal. Calcd for $C_{35}H_{65}O_7PSi$: C, 63.99; H, 9.97. Found: C, 64.04; H, 9.95.

(8*E*)-8,12-Dimethyl-2-(diethylphosphono)-15-hydroxy-12-(methoxymethoxy)-5-isopropenyl-8-pentadecen-13-yn-3-one (22). To a solution of 1.50 g (2.28 mmol) of silyl ether **21** in 10 mL of THF was added 0.26 mL (4.6 mmol) of glacial acetic acid and 4.6 mL (4.6 mmol) of 1.0 M TBAF in THF at 0 °C. The reaction mixture was stirred for 2.5 h at rt, and then it was diluted

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with ether and water, and the layers were separated. The organic layer was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (80–100% EtOAc–hexane) afforded 1.01 g (89%) of alcohol **22**: IR (cm^{-1}, film) 3388, 1716, 1645, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 5.11 (m), 4.96, 4.78 (AB, J = 7.1 Hz), 4.77, 4.79 (AB, J = 0.7 Hz), 4.73, 4.69 (s), 4.29 (s), 4.04–4.15 (m), 3.36 (s), 3.22 (dq, J = 25.2, 7.1 Hz), 3.15 (dq, J = 25.4, 7.1 Hz), 2.54–2.81 (m), 1.65 (s), 1.58 (s), 1.63 (s), 1.57 (s), 1.46 (s), 1.36–1.80 (m), 1.23–1.34 (m). Anal. Calcd for $C_{35}H_{65}O_7PSi$: C, 62.38; H, 9.06. Found: C, 62.21; H, 8.99.

(7*E*)-4,8-Dimethyl-14-(diethylphosphono)-4-(methoxymethoxy)-11-isopropenyl-13-oxo-7-pentadecen-2-ynal (23). The method of Swern was employed[10] as described for aldehyde **10** with 210 μL (2.40 mmol) of oxalyl chloride in 6 mL of CH_2Cl_2 and 230 μL (3.20 mmol) of DMSO at –78 °C to which was added slowly 800 mg (1.60 mmol) of alcohol **22** in 2 mL of CH_2Cl_2 followed after an additional 15 min by 890 μL (6.39 mmol) of triethylamine. The product, 795 mg (99%) of aldehyde **23**, was obtained as a clear yellow oil: IR (cm^{-1}, film) 2211, 1715, 1668, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 9.23 (s), 5.07 (m), 4.93, 4.79 (AB, J = 7.2 Hz), 4.74, 4.70 (s), 4.04–4.16 (m), 3.39 (s), 3.20 (dq, J = 25.3, 7.1 Hz), 3.16 (dq, J = 25.5, 7.1 Hz), 2.03–2.84 (m), 1.65 (s), 1.57 (s), 1.63 (s), 1.54 (s), 1.36–1.89 (m), 1.23–1.34 (m).

(2*Z*,9*E*)-13-Isopropenyl-6-(methoxymethoxy)-2,6,10-trimethyl-2,9-cyclotetradecadien-4-yn-1-one (24). The method of Masamune and Roush was employed.[11] To a stirred suspension of 500 mg (11.8 mmol) of LiCl and 880 μL (5.92 mmol) of DBU in 230 mL of acetonitrile was added 590 mg (1.18 mmol) of phosphonate **23** over 1.5 h. The reaction mixture was stirred for an additional 2 h, and then it was concentrated under reduced pressure and diluted with ether and water, and the layers were separated. The organic layer was washed with 10% HCl and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (10% EtOAc–hexane) afforded 171 mg (42%) of enyne **24** as a 1:1 mixture of diastereomers: IR (cm^{-1}, film) 2360, 1662, 1033.

Isomer a: ^1H NMR (500 MHz, $CDCl_3$) δ 6.51 (s), 5.25 (t, J = 5.3 Hz), 4.79, 5.03 (AB, J = 7.1 Hz), 4.57 (s), 4.73 (s), 3.38 (s), 3.02 (dd, J = 8.7, 11.9 Hz), 2.39 (dd, J = 6.2, 11.9 Hz), 1.81–2.43 (m), 1.35–1.67 (m), 1.92 (s), 1.69 (s), 1.52 (s), 1.49 (s); HRMS calcd for $C_{22}H_{32}O_3$ (M^+) 344.2351, found 344.2347.

Isomer b: ^1H NMR (500 MHz, $CDCl_3$) δ 6.48 (s), 5.25 (t, J = 5.3 Hz), 4.83, 4.98 (AB, J = 7.1 Hz), 4.60 (s), 4.74 (s), 3.39 (s), 2.95 (dd, J = 9.5, 12.2 Hz), 2.46 (dd, J = 4.8, 12.2 Hz), 1.81–2.43 (m), 1.35–1.67 (m), 1.92 (s), 1.69 (s), 1.52 (s), 1.49 (s).

(2*Z*,9*E*)-13-Isopropenyl-6-(methoxymethoxy)-2,6,10-trimethyl-2,9-cyclotetradecadien-4-yn-1-ol (25). The procedure described for alcohol **6** was employed with 145 mg (0.421 mmol) of ketone **24** in 2 mL of Et_2O and 510 μL (0.510 mmol) of a 1.0 M solution of DIBAH in hexane at –78 °C for 15 min. Purification of the product by flash chromatography on silica gel (25% EtOAc–hexane) afforded 136 mg (93%) of allylic alcohol **25** as a mixture of diastereomers. IR (cm^{-1}, film) 3445, 2210, 1644, 1033; ^1H NMR (500 MHz, $CDCl_3$) δ 5.70 (t, J = 1.2 Hz), 5.66 (t, J = 1.2 Hz), 5.16–5.23 (m), 4.83, 5.03 (AB, J = 6.9 Hz), 4.82, 5.03 (AB, J = 6.9 Hz), 4.68–4.74 (m), 4.33 (bs), 3.38 (s), 1.98–2.41 (m), 1.05–1.91 (m), 1.79 (s), 1.78 (s), 1.65 (s), 1.49 (s). Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.14; H, 9.91.

Furan 26. To a solution of 480 mg (1.80 mmol) of 18-crown-6, 1.80 mL (1.80 mmol) of 1.0 M potassium *tert*-butoxide in THF, and 170 μL (1.80 mmol) of *tert*-butyl alcohol was added 125 mg (0.360 mmol) of alcohol **25** in 1 mL of THF. After being stirred for 1.5 h, the reaction mixture was diluted with ether and quenched with 10% aqueous K_2CO_3. The aqueous layer was extracted with ether, and the combined organic layers were washed with 10% aqueous K_2CO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (hexane) afforded 91 mg (88%) of furan **26**: IR (cm^{-1}, film) 1644, 1446, 890; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (d J = 0.9 Hz), 5.83 (s), 5.15–5.33 (m), 4.79 (s), 3.04–3.13 (m), 2.79–2.89 (m), 2.37–2.55 (m), 1.17-2.10 (m), 1.88 (s), 1.85 (d, J = 0.9 Hz), 1.72 (dd, J = 1.1, 0.9 Hz), 1.51 (s), 1.17–1.45 (m); ^{13}C NMR (125 MHz, $CDCl_3$) 151.1, 148.6, 148.4, 136.1, 132.3, 126.2, 116.0, 114.2, 111.7, 111.2, 42.2, 34.1, 33.6, 30.9, 29.2, 26.1, 25.4, 19.4, 18.0, 9.7. Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.32; H, 9.97.

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Supplementary Material Available: Selected ^1H NMR and ^{13}C NMR spectra (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.