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Strictly Regio- and Stereo-Controlled α-Alkenylation of Bicyclic Enone Derivatives *via* Palladium-Catalyzed Cross Coupling and Its Application to a Formal Synthesis of (±)-Carbacyclin[†]

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Abstract:
A formal synthesis of carbacylin was achieved by preparing a known advanced intermediate **15** *via* Zr-promoted enyne bicyclization-carbonylation, Pd-catalyzed α-alkenylation of bicyclic enones, and conjugate reduction.

Keywords: Carbacyclins, Palladium and compounds, Zinc and compounds, Zirconium and compounds

INTRODUCTION

The development of Zr-promoted bicyclization [1,2] of stereo-defined enynes, *e.g.*, conversion of **1** to **2** shown in Scheme 1, prompted us to consider its application to a regio- and stereo-controlled synthesis of carbacyclin [3], a promising anti-blood clotting agent (**3**), as outlined in Scheme 2. Several critical requirements depicted in Scheme 2 included (i) strictly stereoselective synthesis of dienynes represented by **4**, (ii) their conversion to bicyclic intermediates **5** *via* Zr-promoted bicyclization [1], (iii) Pd-catalyzed regio- and stereo-specific cross coupling to give **6**, and (iv) conjugate reduction of **6** with retention of regio- and stereochemical features.

[†] Dedicated to my mentor, colleague, and friend Professor Madeleine M. Joullie in celebration of forty years of distinguished teaching and research at the University of Pennsylvania.

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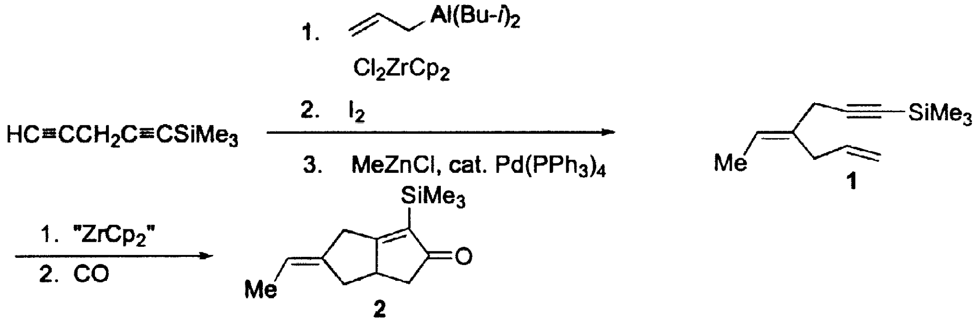
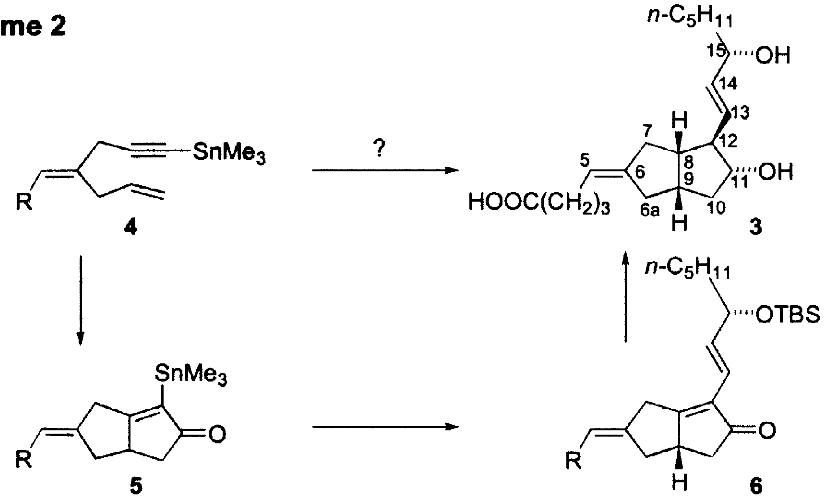
Scheme 1



Scheme 2



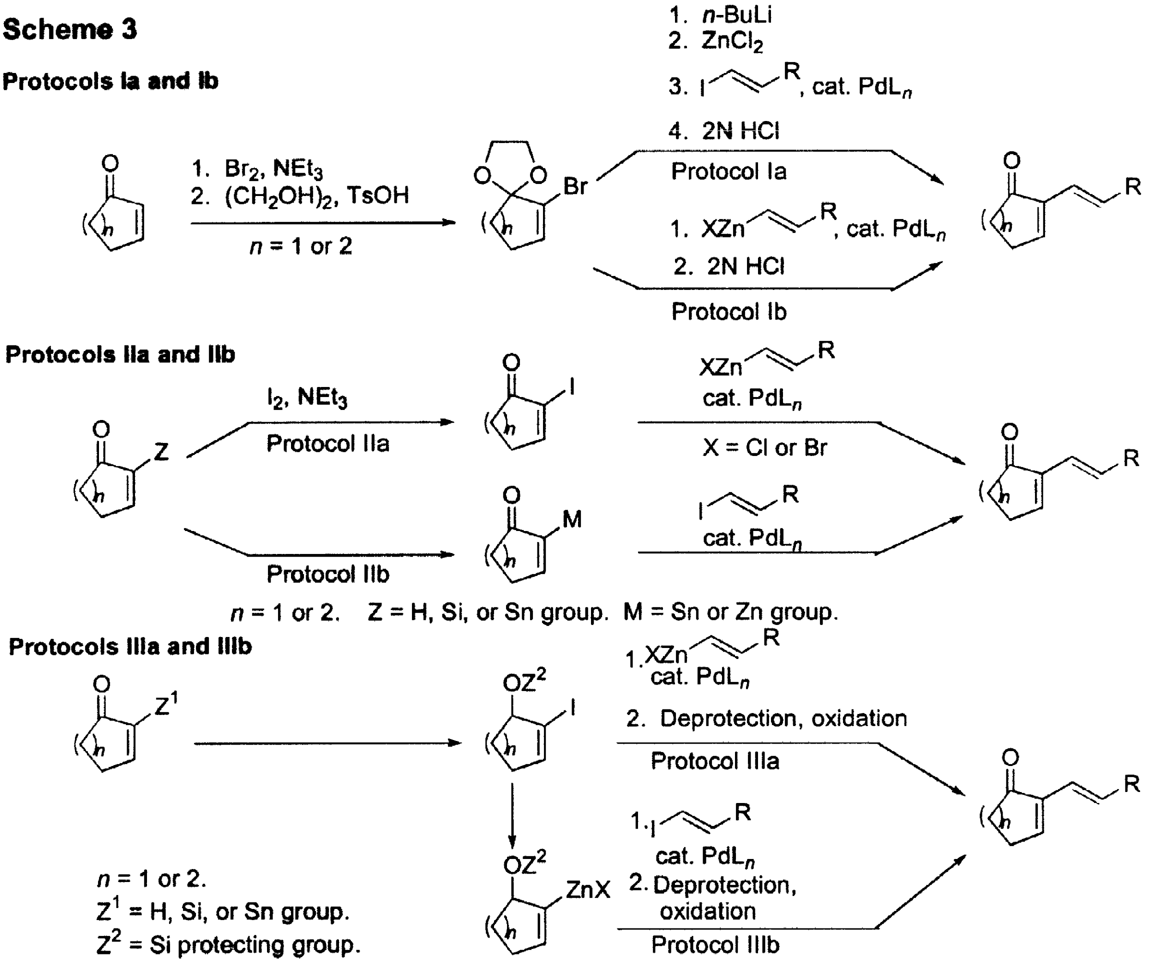
R = $(CH_2)_4OZ^1$, where Z^1 is a protecting group, *e.g.*, THP and TBS.

With Scheme 2 in mind, we then undertook to develop the Pd-catalyzed procedure for regio- and stereo-specific α-alkenylation of enones. Since 1987, we have considered several protocols for this purpose as summarized in Scheme 3 and developed a few of them [4-6]. Of these, Protocols IIa and IIb are the most convenient in that no protection-deprotection of the carbonyl group is required. However, our studies [4] have amply demonstrated that Pd-catalyzed cross coupling of either α-iodo or α-metallo enones is much more demanding than other alkenyl-alkenyl coupling reactions including those involving β-haloenones [4], and it has indeed been necessary to resort to Protocol III in some cases [4c,4d].

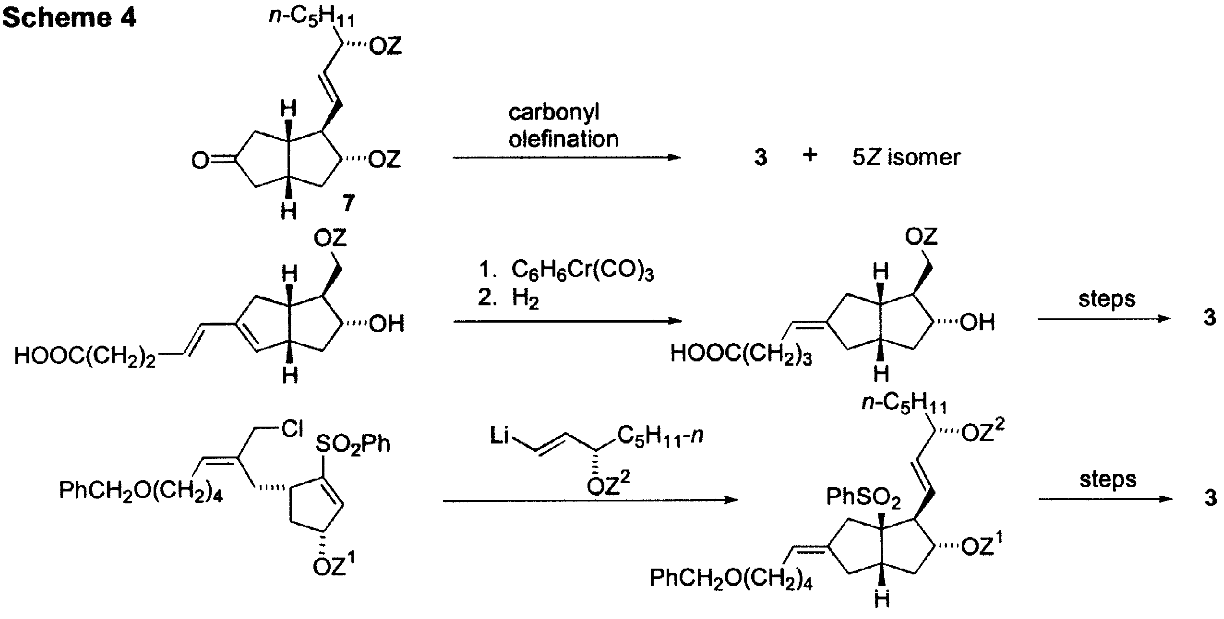
It should be mentioned that most of the earlier syntheses of carbacyclin employed carbonyl olefination of bicyclic intermediate **7** producing mixtures of carbacyclin and its 5*Z* isomer [7]. A few notable exceptions include Shibasaki's Cr-mediated diene-to-monoene conversion [3c,3d] and Fuchs' "triply-convergent" approach with a stereo-defined trisubstituted alkene [3e] (Scheme 4).

In this paper, we describe a strictly regio- and stereo-controlled formal total synthesis of (±)-carbacyclin using Protocol IIIb in the crucial step for alkenyl-alkenyl coupling.

Scheme 3



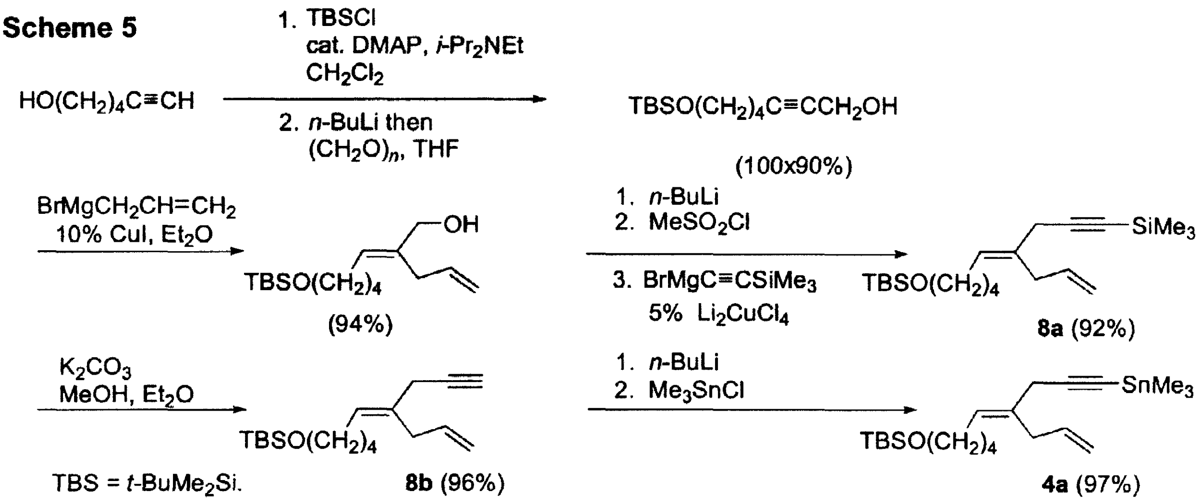
Scheme 4



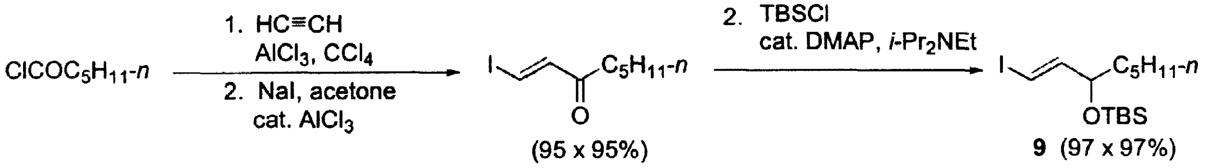
RESULTS AND DISCUSSION

Preparation of Intermediate 4. For the preparation of **4**, two stereoselective routes were considered. One was to convert 1-trimethylsilyl-1,4-pentadiyne to **4** *via* allylalumination [8] catalyzed by Cl_2ZrCp_2 as in Scheme 1. In view of the modest regioselectivity of about 75%, however, a more strictly regio- and stereo-controlled route [1c] shown in Scheme 5 was chosen. Commercially available 5-hexyn-1-ol was successively protected with *t*-$BuMe_2SiCl$ (TBSCl) and hydroxymethylated in 100 and 90% yields, respectively. Allylmagnesiation of the propargylic alcohol catalyzed by 10 mol % of CuI [9] provided the desired dienol in 94% with essentially complete control of regio- and stereochemistry. After conversion of the product to its mesylate, Cu-catalyzed ethynylation with $Me_3SiC{\equiv}CMgBr$ [10] gave **8a** in 92% yield, which was converted to **8b** in 96% yield by treatment with K_2CO_3 in MeOH-Et_2O. Successive treatment of **8b** with *n*-BuLi and Me_3SnCl gave **4a** in 97% yield (73% overall from 5-hexyn-1-ol). The preparation of **9** was achieved as shown in Scheme 6 by known methods [11,12] described previously in detail [13].

Scheme 5

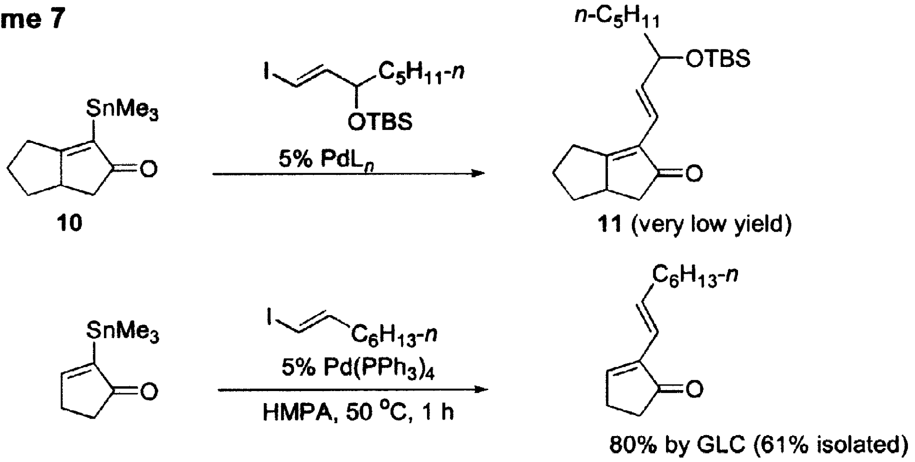


Scheme 6



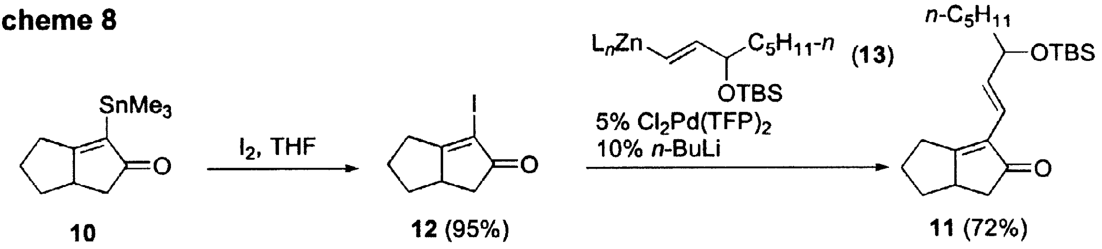
Attempted Synthesis of Carbacyclin Using Protocol II. One highly efficient route to carbacyclin (**3**) *via* **4a** would be to convert **4a** to **5a** (Z′ = TBS, cf. Scheme 9) and achieve cross coupling between **5a** and **9** in the presence of a Pd catalyst. However, our earlier attempts [4b] to achieve Pd-catalyzed cross coupling between a model bicyclic compound **10** [1d] and **9** led only to very low yields of the desired compound **11**, even though the corresponding reaction of 2-(trimethylstannyl)-2-cyclopentenone with (*E*)-1-iodo-1-octene proceeded in 80% GLC yield (61% isolated) (Scheme 7). Even the use of a more recent and improved procedure employing Pd(dba)$_2$, AsPh$_3$, CuI, and *N*-methylpyrrolidinone [14a] led only to a complex product mixture. These results indicated that the required cross coupling of the chemically labile and sterically demanding tetrasubstituted alkenyl derivative **5a** with **9** must be rather difficult.

Scheme 7



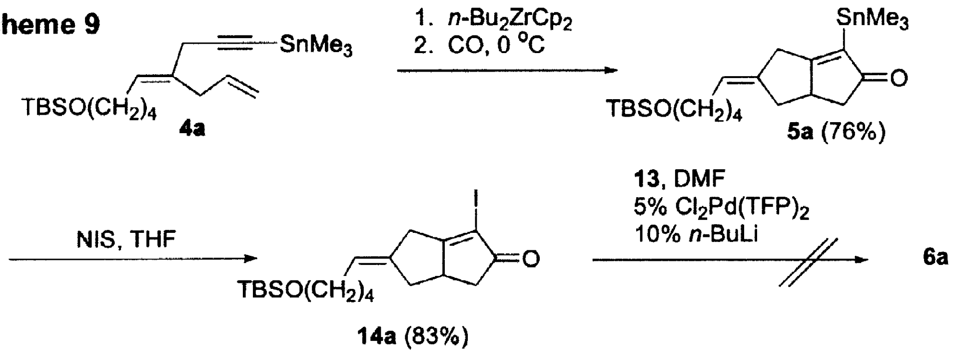
In marked contrast, the Pd-catalyzed cross coupling between α-iodoenone **12** and a Zn derivative (**13**) of **9** (Protocol IIa) was very favorable (Scheme 8), as suggested by related earlier results [4b]. Thus, iodoenone **12** was prepared in 95% yield by treatment of **10** with 1.1 equiv of iodine in THF. Its cross coupling with **13** (prepared by successive treatment of **9** with *n*-BuLi and dry ZnBr$_2$ (0.5 molar equiv) followed by evaporation and addition of DMF) catalyzed by a Pd complex, generated *in situ* by treatment of 5 mol % of Cl$_2$Pd(TFP)$_2$, where TFP is tris(*o*-furyl)phosphine, with 10 mol % of *n*-BuLi, led to a 72% yield of a diastereomeric mixture of **11**. The superiority of TFP [14] relative to PPh$_3$ was previously observed [4b].

Scheme 8



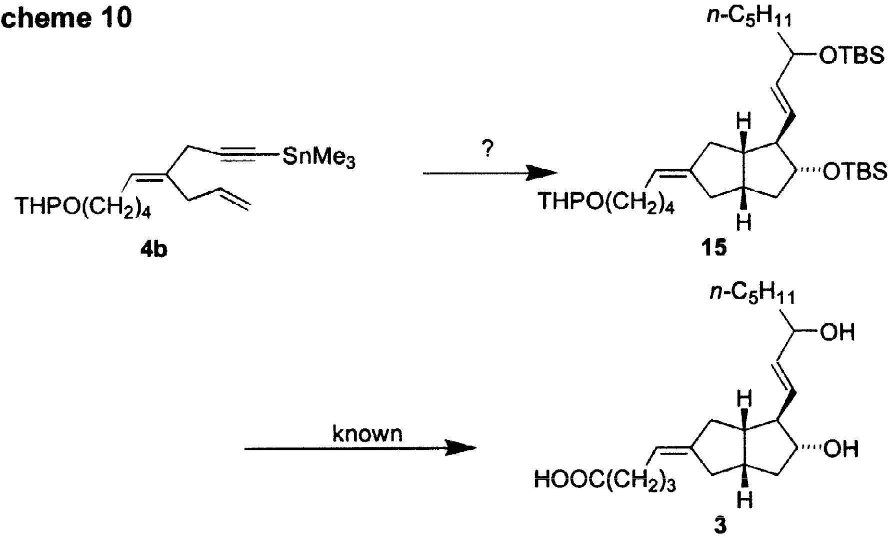
The Zr-promoted bicyclization-carbonylation of **4a** initially gave variable yields of **5a**. It was soon found that *the reaction of Cl$_2$ZrCp$_2$ with n-BuLi to give (n-C$_4$H$_9$)$_2$ZrCp$_2$ must be completed by warming the mixture to -25 °C for several minutes with efficient stirring before addition of* ***4a*** *to minimize side reactions.* With this precaution, conversion of **4a** to **5a** was achieved reproductively in over 70% yield (max. 76%). For the conversion of **5a** to **14a**, the use of *N*-iodosuccinimide (NIS) proved to be preferable to that of I_2. To our disappointment, attempts to achieve cross coupling between **13** and **14a** did not produce significant amounts (5% or more) of the desired compound **6a** under the conditions that were satisfactory for the conversion of **12** to **11** (Scheme 8). The starting iodoenone **14a** was consumed within 20 min under the reaction conditions. These results are summarized in Scheme 9.

Scheme 9



Formal Total Synthesis of Carbacyclin (3). Conversion of 4b to 15. Recent development of a more general, albeit more elaborate, protocol (Protocol IIIb) for more demanding cases of Pd-catalyzed α-alkenylation of enones [4c,4d] prompted us to apply this protocol to the synthesis of carbacyclin. Since **15** was previously synthesized and converted to carbacyclin [3b], we chose **15** as our synthetic target.

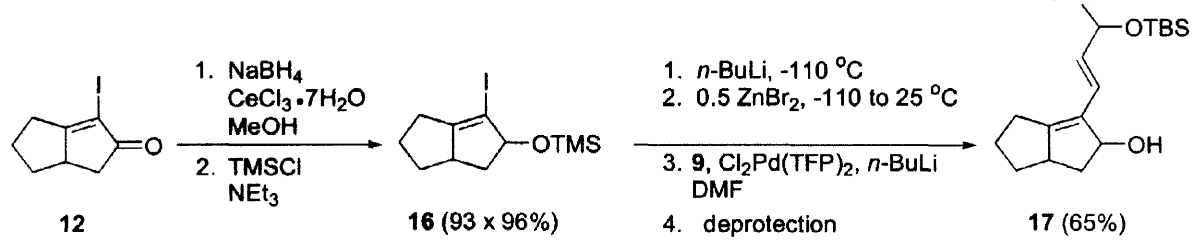
Scheme 10



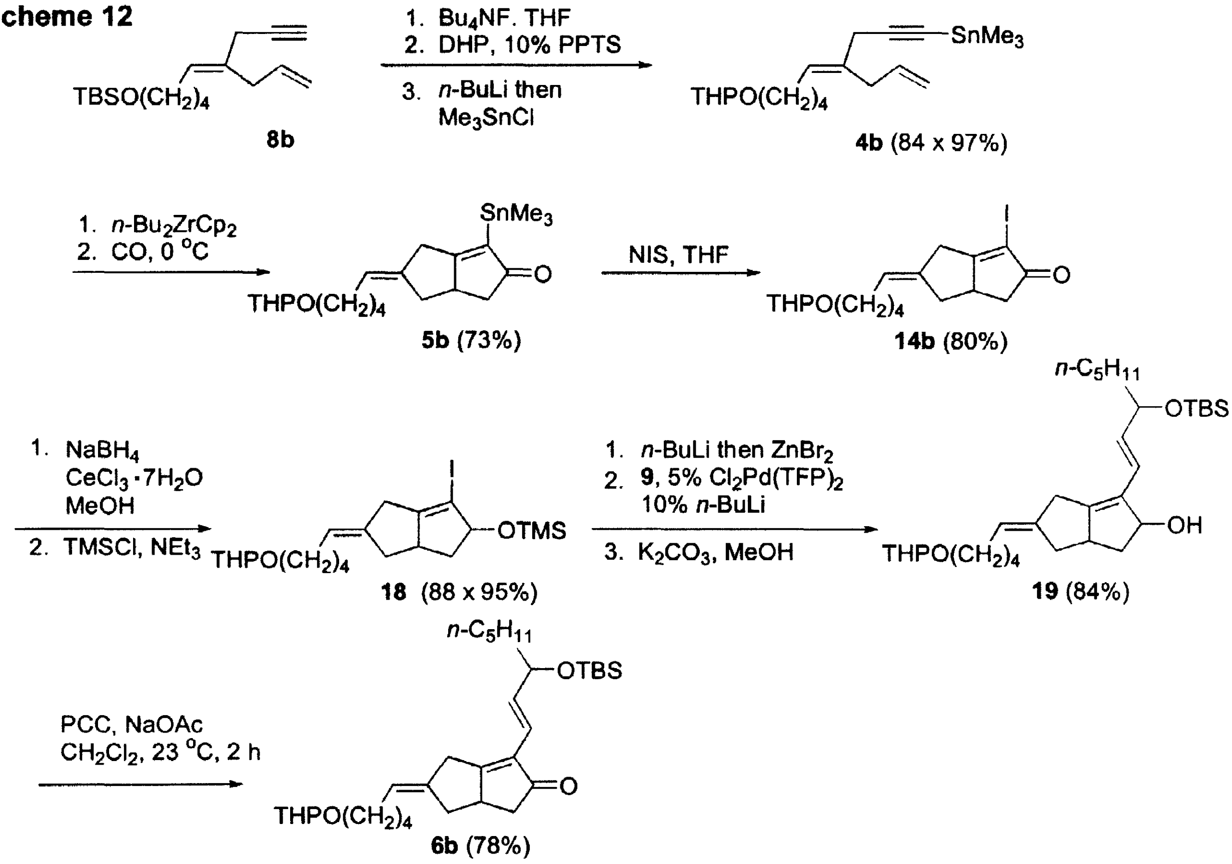
To probe the applicability of Protocol IIIb (Scheme 3) to the required Pd-catalyzed cross coupling, iodoenone **12** was reduced with $NaBH_4$ and $CeCl_3{\cdot}7H_2O$ [15] to give **16** after treatment with Me_3SiCl in 89% combined yield. Conversion of **16** to a Zn derivative and Pd-catalyzed cross coupling with **9** using the same conditions as those for the conversion of **12** to **11** proceeded to give, after protonolysis with K_2CO_3 in MeOH, **17** in 65% yield as a diastereoisomeric mixture.

The use of PPh_3 in place of TFP led to a yield of 53% (Scheme 11).

Scheme 11



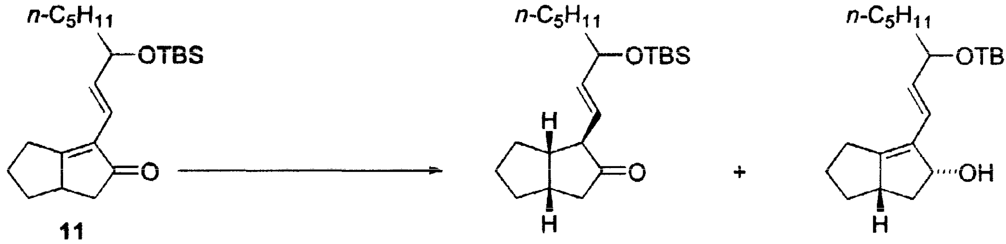
Scheme 12



For the synthesis of **15**, **8b** was first converted to **4b** by removal of the TBS group of **8b** with Bu_4NF in THF followed by the standard THP protection with dihydropyran (DHP) and pyridinium *p*-toluenesulfonate (PPTS) in 84% yield and stannylation in 97% yield. The Zr-promoted bicyclization-carbonylation [1] gave **5b** in 73% yield, and its iodinolysis with NIS to give **14b** proceeded in 80% yield. Reduction of **14b** with $NaBH_4$ and $CeCl_3{\cdot}7H_2O$ [15] followed by TMS protection provided **18** in 84% combined yield. The Pd-catalyzed cross-coupling reaction of a Zn derivative of **18** with **9** under the same conditions as those for successful conversion of **12** to **11** and that of **16** to **17** as well as attempted but unsuccessful conversion of **14a** to **6a** proceeded in 90% NMR yield. After selective deprotection of the TMS group with K_2CO_3 and MeOH, a diastereomeric mixture of **19** was obtained in 84% isolated yield based on **18**. Oxidation of **19** with 3 equiv each of PCC and NaOAc in CH_2Cl_2 provided a diastereomeric mixture of **6b** in 78% yield (Scheme 12).

Conjugate reduction of **6b** has proved to be the most difficult step in the entire synthesis, which remains to be further improved. In an attempt to find a satisfactory procedure, several known reactions were screened using **11** as a test system. To our disappointment, none turned out to be highly satisfactory. The Birch-type reduction [16] using Li, NH_3, *t*-BuOH, and THF at -33 °C gave **20** in 46% NMR yield along with about 20% yield of the 1,2-reduction product **17** and some unidentified byproducts. A reagent combination consisting of $LiAlH(OMe)_3$ and CuBr [17] provided **20** and **17** in 28 and 39% yields, respectively (Scheme 13). On the other hand, DIBAL-H (4 equiv) in the presence of 10 mol % of MeCu [18] in HMPA-THF at -50 °C gave **20** in only 8% NMR yield, while $(CuH{\cdot}PPh_3)_6$ [19] and *n*-BuLi-DIBAL-H used in conjunction with tris(2,6-diphenylphenoxy)aluminum [20] led to complex product mixtures.

Scheme 13



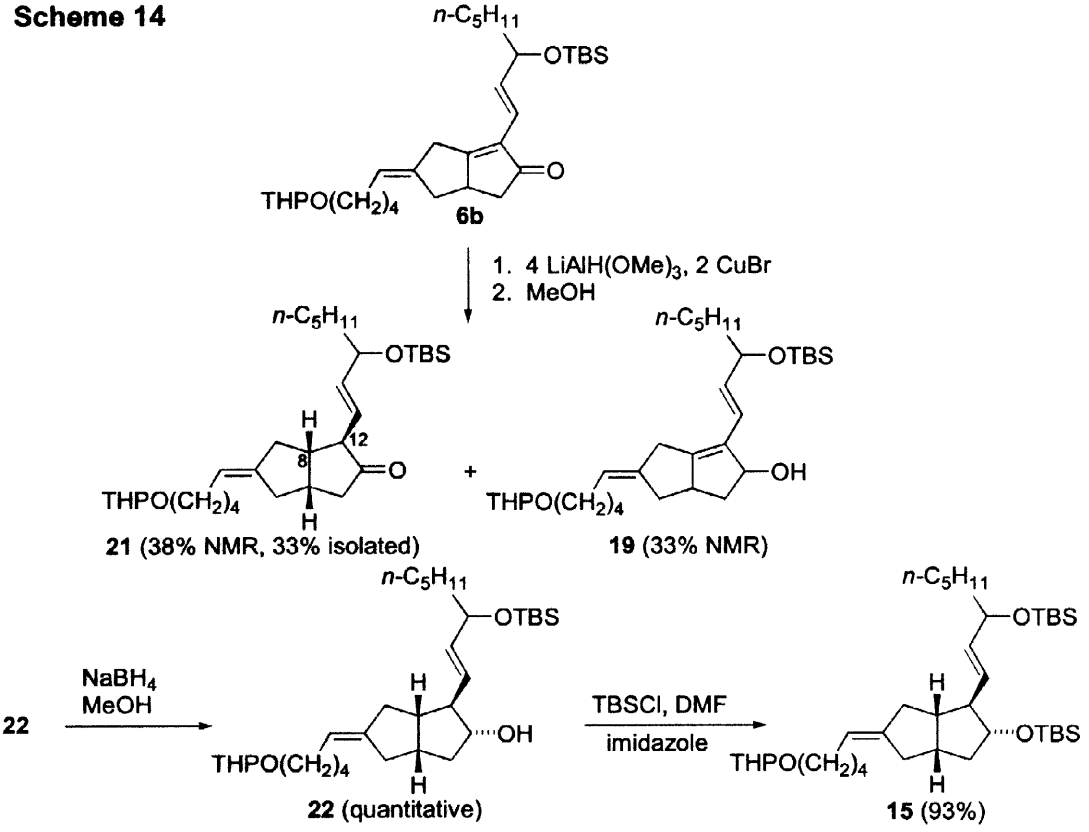
11

Reagents	**20**	**17**
Li, NH_3, *t*-BuOH, THF	46%	20%
$LiAlH(OMe)_3$, CuBr	28%	39%

In the reduction of **6b**, the Birch-type reduction led to a complex product mixture, which may, in part, be due to the relatively high acidity of **6b**. On the other hand, treatment of **6b** with 4 equiv of $LiAlH(OMe)_3$ and 2 equiv of CuBr in THF at -78 to -20 °C followed by quenching with an excess of MeOH at -20 to 23 °C provided a relatively clean product mixture containing the desired **21** and the 1,2-reduction product **19** as diastereomeric mixtures in 38 and 33% NMR yields, respectively. The other products were present only in very minor amounts. The stereoselectivity in the generation of the C-8 and C-12 chiral carbon atoms must be very close to 100%. In view of the presence of three C=C bonds, selective reduction of the tetrasubstituted double bond without involving competitive migration and/or reduction of the other two C=C bonds is noteworthy. As in the previously reported cases [4a,4b] protonation of the putative metal dienolate intermediate with MeOH must selectively occur in the α position. A diastereomeric mixture of **21** free of other species was isolated in 33% yield. Since **19** can be oxidized to regenerate **6b**, the yield of **21** can be further improved. This, however, was not performed.

Reduction of a diastereomeric mixture of **21** with $NaBH_4$ afforded a clean diastereomeric mixture of **22** in essentially quantitative yield, indicating a nearly exclusive *exo*-side attack of the carbonyl group by $NaBH_4$. Protection of the hydroxyl group with TBSCl in DMF in the presence of imidazole provided **15** as a diastereomeric mixture in 93% yield (Scheme 14). Its ^1H and ^{13}C NMR spectral data are in agreement with those reported in the literature [3b]. Even if **15** is diastereochemically homogeneous with respect to the four asymmetric carbon centers in the bicyclic frame as claimed here, it must consist of four diastereomers. However, the sole asymmetric carbon center of the THP group is sufficiently remote from the other asymmetric carbon atoms so that it does not complicate the NMR spectra, thereby permitting its identification by spectral comparison.

Scheme 14



CONCLUSIONS

1. A novel protocol for an efficient construction of the bicyclic framework of carbacyclin with simultaneous incorporation of the *exo-alkylidene* side chain of the correct *E* geometry *via* Zr-promoted enyne bicyclization-carbonylation has been developed.

2. The applicability of various protocols for α-alkenylation of enones to the introduction of the alkenyl side chain of carbacyclin has been examined. Protocol IIIb as defined in Scheme 3 has been found to permit the required synthetic task selectively and in high yield, whereas more efficient Protocols IIa and IIb, which are satisfactory in the α-alkenylation of monocyclic enones,

have not yielded satisfactory results. These results point to the inherent difficulties associated with α-alkenylation of enones and the need for further developments in this area.

3. A formal total synthesis of (±)-carbacyclin was achieved by the preparation of a known advanced intermediate **15** *via* conjugate reduction of **6b** and carbonyl reduction. The conjugate reduction step proved to be by far the least satisfactory step in the synthesis, which points to the need for developing more satisfactory procedures for 1,4-reduction of bicyclic enones.

4. This study also acutely points to the desirability of developing Zr-catalyzed enantioselective enyne bicyclization procedures.

EXPERIMENTAL

General Procedures. Manipulation involving organometallics were carried out under an atmosphere of N_2 or Ar using standard techniques [21]. Organolithium and organomagnesium halides were titrated with either menthyl 2,2′-bipyridyl or 2-butanol/1,10-phenanthroline [22]. Gas chromatographic measurements were performed on SE-30 (Chromosorb W) columns. THF and diethyl ether were distilled from sodium benzophenone ketyl; CH_2Cl_2 from P_2O_5; hexane and benzene from $LiAlH_4$; toluene, DMF, CH_3CN, and Et_3N from CaH_2; HMPA from triphenylmethyllithium. After distillation from their respective drying agents, all solvents were stored over 4 Å molecular sieves. $ZnCl_2$, LiBr, and NaI were dried at 100 °C at ≤0.5 mm Hg for 4-6 h. Dichlorobis(tris-2-furylphosphine)palladium [14], $LiAlH(OMe)_3$-CuBr [17], MeCu [18], $(CuH{\cdot}PPh_3)_6$ [19], and tris(2,6-diphenylphenoxy)aluminum [20] were prepared as described in the corresponding references. Acetylene from a cylinder was purified by passing it through water, H_2SO_4, KOH pellets, and a trap kept at -78 °C. All other commercial reagents were used as received.

(*E*)-1-Iodo-3-(*t*-butyldimethylsilyloxy)-1-octene (9) [11] was prepared as previously described in detail [13].

7-(Trimethylstannyl)-1-hepten-6-yne, 2-(trimethylstannyl)-bicyclo[3.3.0]oct-1(2)-en-3-one (10), and 2-Iodobicyclo[3.3.0]oct-1(2)-en-3-one (12) were also prepared as previously described in detail [1d].

6-(*t*-Butyldimethylsilyloxy)-1-hexyne. To a solution of *t*-butyldimethylsilyl chloride (16.58 g, 110 mmol), Et_3N (16.73 mL, 12.14 g, 120 mmol) and 4-dimethylaminopyridine (0.61 g, 5 mmol) in CH_2Cl_2 (100 mL) was added 5-hexyn-1-ol (9.8 g, 100 mmol) in CH_2Cl_2 (20 mL) and 0 °C. The reaction mixture was then stirred at room temperature for 20 h and poured into saturated aqueous NH_4Cl. Extraction with ether, washing with aqueous $NaHCO_3$ and brine, drying ($MgSO_4$), concentration, and distillation provided 21.2 g (100%) of the title compound: bp 74 °C (3 mm Hg); ^1H NMR ($CDCl_3$, C_6H_6) δ -0.05 (s, 6 H), 0.82 (s, 9 H), 1.4-1.6 (m, 4 H), 1.75-1.85 (m, 1 H), 2.0-2.2 (m, 2 H), 3.45-3.65 (m, 2 H); IR (neat) 3320 (m), 1105 (s), 840 (s), 775 (s) cm^{-1}.

7-(*t*-Butyldimethylsilyloxy)-2-heptyn-1-ol. To 6-(*t*-butyldimethylsiloxy)-1-hexyne (21.2 g, 100 mmol) in THF (200 mL) was added at -78 °C *n*-BuLi in hexane (2.63 M, 39.9 mL, 105 mmol) and paraformaldehyde (9 g, 300 mmol) as a slurry in THF (100 mL). The resultant mixture was warmed to 23 °C, stirred overnight, and poured into a mixture of ether, ice and 3N HCl. After extraction with ether, the organic layer was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, concentrated, and distilled to provide 21.8 g (90%) of the title compound: bp 100 °C (2 mm Hg; ^{1}H NMR ($CDCl_3$, C_6H_6) δ -0.05 (s, 6 H), 0.80 (s, 9 H), 1.4-1.6 (m, 4 H), 2.1-2.2 (m, 2 H), 2.77 (bs, 1 H), 3.53 (t, J = 6 Hz, 2 H), 4.11 (s, 2 H); IR (neat) 3600-3100 (m), 1105 (s), 840 (s), 775 (s) cm^{-1}.

(*E*)-2-Allyl-7-(*t*-butyldimethylsilyloxy)-2-hepten-1-ol. Allylmagnesium bromide in ether (0.98 M, 210 mL, 206 mmol), was added dropwise at 0 °C to a solution of 7-(*t*-butyldimethylsilyloxy)-2-heptyn-1-ol (19.94 g, 82.4 mmol) and copper iodide (1.6 g, 8.4 mmol) in ether (85 mL). After stirring for 18 h at 23 °C, the mixture was hydrolyzed at 0 °C with saturated NH_4Cl. The aqueous layer was extracted with ether, the combined organic layers were washed with aqueous $NaHCO_3$ and brine, and then dried over $MgSO_4$. Concentration and distillation provided 22 g (94%) of the title compound: bp 100-105 °C (0.06 mm Hg); ^{1}H NMR ($CDCl_3$, C_6H_6) δ -0.05 (s, 6 H), 0.80 (s, 9 H), 1.25-1.5 (m, 4 H), 1.9-2.0 (m, 2 H), 2.74 (d, J = 6 Hz, 2 H), 3.51 (t, J = 6 Hz, 2 H), 3.88 (s, 2 H), 4.85-5.0 (m, 2 H), 5.35-5.45 (m, 1 H), 5.6-5.75 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -5.43, 18.19, 25.76, 25.83, 27.11, 32.27, 32.36, 62.89, 66.51, 115.11, 127.54, 135.77, 136.37 ; IR (neat) 3600-3100 (m), 3080 (w), 1640 (w), 1100 (s), 835 (s), 775 (m) cm^{-1}.

(*E*)-1-(Trimethylsilyl)-4-allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (8a). (*E*)-2-Allyl-7-(*t*-butyldimethylsilyloxy)-2-hepten-1-ol (18.2 g, 64.1 mmol) in THF (65 mL) was sequentially treated at -78 °C with *n*-BuLi in hexane (2.43 M, 29 mL, 70.5 mmol), CH_3SO_2Cl (8.08 g, 5.46 mL, 70.5 mmol), and $Me_3SiC{\equiv}CMgBr$ (89.7 mmol) in THF (90 mL) in the presence of Li_2CuCl_4 (0.1 M, 32 mL, 3.2 mmol) [10]. The mixture was warmed to 25 °C over 2 h, stirred for an additional hour, quenched with saturated NH_4Cl and pentane. The aqueous layer was extracted with pentane, and the combined organic layers were washed with aqueous $NaHCO_3$ and brine. After drying over $MgSO_4$, concentration and column chromatography (silica gel, 90/10 pentane-Et_2O) afforded 21.5 g (92%) of the title compound: ^{1}H NMR ($CDCl_3$, C_6H_6) δ -0.05 (s, 6 H), 0.06 (s, 9 H), 0.80 (s, 9 H), 1.25-1.5 (m, 4 H), 1.95-2.05 (m, 2 H), 2.73 (d, J = 1 Hz, 2 H), 2.82 (s, 2 H), 3.45-3.55 (m, 2 H), 4.85-5.0 (m, 2 H), 5.4-5.5 (m, 1 H), 5.55-5.7 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -5.30, 0.10, 18.31, 25.95, 27.48, 27.53, 32.49, 34.65, 62.99, 86.95, 104.56, 115.63, 127.48, 131.24, 135.42; IR (neat) 3092 (w), 2040 (s), 1640 (w), 1250 (s), 1100 (s), 840 (s), 775 (s) cm^{-1}. Anal. calcd for $C_{21}H_{40}OSi$: C, 69.16; H, 11.06. Found: C, 69.08; H, 11.24.

(*E*)-4-Allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (8b). To 1-(trimethylsilyl)-4-allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (14.56 g, 40 mmol) in MeOH (80 mL) and Et_2O (20 mL) was added K_2CO_3 (6.08 g, 44 mmol). The reaction mixture was stirred at 23 °C for 12 h, quenched with saturated aqueous NH_4Cl, extracted with ether, washed with aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), concentrated, and distilled to provide 11.2 g (96%) of the title compound: bp 86-90 °C (1 mm Hg); ^1H NMR ($CDCl_3$, C_6H_6) δ -0.06 (s, 9 H), 0.79 (s, 9 H), 1.2-1.5 (m, 4 H), 1.9-2.0 (m, 3 H), 2.7-2.8 (m, 4 H), 3.50 (t, *J* = 6 Hz, 2 H), 4.85-5.0 (m, 2 H), 5.4-5.5 (m, 1 H), 5.5-5.7 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -5.56, 18.13, 25.79, 27.37, 32.35, 34.36, 62.97, 70.43, 81.94, 115.82, 127.81, 131.24, 135.50 ; IR (neat) 3320 (m), 3080 (w), 2120 (w), 1640 (w), 1100 (s), 835 (s), 775 (s) cm^{-1}. Anal. calcd for $C_{18}H_{32}OSi$: C, 73.91; H, 11.02. Found: C, 74.12; H, 11.05.

(*E*)-1-(Trimethylstannyl)-4-allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (4a). To (*E*)-4-allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (1.46 g, 5 mmol) in THF (5 mL) was added *n*-BuLi in hexane (2.3 M, 2.18 mL, 5 mmol) at -78 °C. The reaction mixture was stirred for 1 h, and Me_3SnCl (1.04 g, 5.2 mmol) in THF (5 mL) was added. The reaction mixture was warmed to 23 °C and stirred overnight. Concentration, dilution with pentane, filtration over Celite, drying ($MgSO_4$), filtration (Celite), concentration, and evacuation of all volatiles at 0.5 mm Hg for 12 h provided 2.20 g (97%) of the title compound: ^1H NMR ($CDCl_3$, C_6H_6) δ -0.06 (s, 6 H), 0.16 (s, 9 H), 0.79 (s, 9 H), 1.25-1.35 (m, 2 H), 1.35-1.5 (m, 2 H0, 1.9-2.0 (m, 2 H), 2.73 (d, *J* = 3 Hz, 2 H), 2.84 (s, 2 H), 3.50 (t, *J* = 6 Hz, 2 H), 4.85-5.0 (m, 2 H), 5.4-5.5 (m, 1 H), 5.55-5.7 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -7.91, -5.35, 18.24, 25.89, 27.48, 27.66, 32.44, 34.56, 62.93, 84.74, 107.67, 115.47, 127.19, 131.55, 135.45; IR (neat) 3080 (w), 1640 (s), 1100 (s), 840 (s), 765 (s) cm^{-1}.

(*E*)-4-Allyl-9-tetrahydropyranyloxy-4-nonen-1-yne. To a solution of (*E*)-4-allyl-9-(*t*-butyldimethylsilyloxy)-4-nonen-1-yne (2.14 g, 7.3 mmol) in THF (7 mL) was added 1M Bu_4NF in THF (11 mL, 11 mmol) at 0 °C. The reaction mixture was warmed to 23 °C and stirred for 4 h. The solvent was evaporated. The residue was dissolved in Et_2O/hexane (1:1), and filtered through a short column of silica gel. The crude alcohol was dissolved and in CH_2Cl_2 (15 mL), and dihydropyran (1.23 g, 14.6 mmol) and pyridinium *p*-toluenesulfonate (184 mg, 0.73 mmol) were added to the solution. After 2 h at 23 °C, the reaction mixture was diluted with Et_2O and washed with 0.5N HCl, H_2O, and saturated $NaHCO_3$. The organic phase was dried over $MgSO_4$ and concentrated. Chromatography on silica gel (30/70 ether-hexane) afforded the title compound (1.61 g, 84%) as an oil: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.35-1.9 (m, 10 H), 2.0-2.15 (m, 3 H), 2.8-2.95 (m, 4 H), 3.3-3.55 (m, 2 H), 3.65-3.95 (m, 2 H), 4.5-4.6 (m, 1 H), 4.95-5.1 (m, 2 H), 5.56 (5, *J* = 7.3 Hz, 1 H), 5.6-5.85 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.50, 25.37, 25.84, 26.21, 27.45, 29.27, 30.61, 34.39, 62.07, 67.24, 70.43, 81.78, 98.62, 115.62, 127.39, 131.02, 135.20; IR (neat) 3308 (s), 1638 (m) cm^{-1}; MS (m/z) 263 $(M+H)^+$, 179, 161, 85 (100).

(*E*)-4-Allyl-1-(trimethylstannyl)-9-tetrahydropyranyloxy-4-nonen-1-yne (4b). This compound was prepared in a manner similar to that for the preparation of **4a** using (*E*)-4-allyl-9-

tetrahydropyranyloxy-4-nonen-1-yne (1.61 g, 6.13 mmol), *n*-BuLi in hexane (2.5 M, 2.58 mL, 6.45 mmol), and Me_3SnCl in THF (1 M, 6.75 mL, 6.75 mol). The title compound obtained in 97% yield (2.53 g) was characterized by ^1H NMR and used in the subsequent step: ^1H NMR (C_6D_6, Me_4Si) δ 0.17 (s, 9 H), 1.15-1.9 (m, 10 H), 1.9-2.1 (m, 2 H), 2.83 (bd, J = 6.6 Hz, 2 H), 2.95-3.05 (m, 2 H), 3.2-3.5 (m, 2 H), 3.7-3.9 (m, 2 H), 4.58 (t, J = 3.3 Hz, 1 H), 4.85-5.1 (m, 2 H), 5.55-5.8 (m, 2 H).

(*E*)-7-(5′-*t*-Butyldiemthylsilyloxy)pentylidene-2-(trimethylstannyl)bicyclo[3.3.0]oct-1(2)-en-3-one (5a). To Cp_2ZrCl_2 (0.614 g, 2.1 mmol) suspended in THF (7 mL) was added at -78 °C *n*-BuLi in hexane (2.35 M, 1.79 mL), 4.2 mmol). The mixture was warmed to -25 °C to complete the formation of *n*-Bu_2ZrCp_2 and cooled again to -78 °C. To this was added (*E*)-1-(trimethylstannyl)-4-allyl-9-(*t*-butyldimethylsilylox)-4-nonen-1-yne (0.91 g, 2.0 mmol) in toluene (3 mL). The reaction mixture was warmed to 23 °C and stirred for 3 h. After cooling to 0 °C, the reaction system was charged with CO and stirred for 3 h. The reaction mixture was diluted with Et_2O and quenched at 0 °C with 3N HCl. Extraction with Et_2O, washing with aqueous $NaHCO_3$ and brine, drying over Na_2SO_4, concentration at 0.1 mm Hg at 23 °C, and chromatography on silica gel (15/85 EtOAc-hexane) afforded 0.90 g (93%) of the title compound: ^1H NMR ($CDCl_3$, C_6H_6) δ -0.05 (s, 6 H), 0.15 (s, 9 H), 0.80 (s, 9 H), 1.25-1.5 (m, 4 H), 1.65-1.5 (m, 1 H), 1.85-2.05 (m, 2 H), 2.5-2.6 (m, 1 H), 2.7-3.0 (m, 2 H), 3.1-3.2 (m, 2 H), 3.51 (t, J = 6 Hz, 2 H), 5.25-5.35 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -9.54, -5.33, 18.27, 25.63, 25.90, 28.85, 32.37, 35.12, 35.65, 42.96, 47.71, 62.96, 124.40, 136.76, 138.22, 196.72, 214.98; IR (neat) 1695 (s), 1615 (m), 1250 (m), 1100 (s), 840 (s), 775 (s) cm^{-1}. High resolution MS calcd for $C_{22}H_{40}O_2SiSn$ (+H-CH_4) 465.1583, found 465.1576.

(*E*)-7-(5′-Tetrahydropyranyloxypentylidene)-2-(trimethylstannyl)bicyclo[3.3.0]oct-1(2)-en-3-one (5b). This compound was prepared in a manner similar to that for the preparation of **5a** using Cp_2ZrCl_2 (1.91 g, 6.54 mmol), *n*-BuLi (2.5 M, 5.33 mL, 13.33 mmol), and (*E*)-4-allyl-9-(5′-tetrahydropyranyloxypentylidene)-1-(trimethylstannyl)-4-nonen-1-yne (2.53 g, 5.95 mmol). The title compound was obtained as an oil (1.97 g, 73%): ^1H NMR (C_6D_6) δ 0.32 (s, 9 H), 1.1-2.0 (m, 14 H), 2.3-2.55 (m, 3 H), 2.85-3.15 (m, 2 H), 3.25-3.5 (m, 2 H), 3.75-3.95 (m, 2 H), 4.60 (t, J = 3.4 Hz, 1 H), 5.15-5.3 (m, 1 H); ^{13}C NMR (C_6D_6) δ -9.51 (3C), 19.74, 25.93, 26.66, 29.28, 29.88, 31.08, 35.21, 35.68, 42.86, 47.78, 61.70, 67.34, 98.71, 124.21, 137.05, 138.91, 195.04, 212.93; IR (neat) 1690 (s), 1612 (s). High resolution MS calcd for $C_{21}H_{34}O_3Sn^{116}$ 451.1603, found 451.1598.

(*E*)-2-Iodo-7-(5′-*t*-butyldimethylsilyloxypentylidene)bicyclo[3.3.0]oct-1(2)-en-3-one (14a). To **5a** (2.42 g, 5 mmol) in THF (5 mL) at -78 °C was added *N*-iodosuccinimide (1.35 g, 6 mmol) in THF (5 mL). The reaction mixture was stirred at -78 °C for 30 min, warmed to 0 °C, quenched with aqueous $NaHCO_3$, washed with brine, dried ($MgSO_4$), and concentrated. Flash chromatography (9/1 pentane-EtOAc) provided 1.86 g (83%) of the title compound: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.35-1.6 (m, 4 H), 1.85-2.1 (m, 3 H), 2.2-2.3 (m, 1

H), 2.8-3.05 (m, 2 H), 3.1-3.2 (m, 1 H), 3.25-3.35 (m, 2 H), 3.61 (5, *J* = 6 Hz, 2 H), 5.4-5.5 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -5.51, 18.05, 25.38, 25.71, 28.75, 32.14, 35.21, 36.40, 40.25, 46.30, 62.66, 93.51, 125.46, 135.44, 190.76, 203.51; IR (neat) 1716 (s), 1632 (s), 1606 (s) cm^{-1}. High resolution MS Calcd for $C_{19}H_{31}IO_2Si$ 447.1216, found 447.1209.

(*E*)-2-Iodo-7-(5′-tetrahydropyranyloxypentylidene)bicyclo[3.3.0]oct-1(2)-en-3-one(14b). This compound was prepared in a manner similar to that for the preparation of **14a** using **5b** (1.90 g, 4.2 mmol) and *N*-iodosuccinimide (1.23 g, 5.47 mmol). Flash chromatography on silica gel (30/70, Et_2O-hexane) afforded the title compound as an oil (1.4 g, 80%): ^{1}H NMR (C_6D_6) δ 0.9-1.15 (m, 1 H), 1.15-1.9 (m, 13 H), 2.05-2.35 (m, 3 H), 2.68 (d, *J* = 21.5 Hz, 1 H), 2.87 (d, *J* = 21.5 Hz, 1 H), 3.25-3.45 (m, 2 H), 3.75-3.95 (m, 2 H), 4.60 (t, *J* = 3.4 Hz, 1 H), 5.0-5.15 (m, 1 H); ^{13}C NMR (C_6D_6) δ 19.78, 25.91, 26.51, 29.27, 29.83, 31.09, 35.03, 36.40, 40.21, 46.20, 61.81, 67.34, 94.75, 98.78, 125.01, 136.48, 189.36, 202.10; IR (neat) 1714 (s), 1632 (s) cm^{-1}; High resolution MS calcd for $C_{18}H_{25}IO_3$ (+H) 417.0927, found 417.0918.

(*E*)-3-Hydroxy-2-iodo-7-(5′-tetrahydropyranyloxypentylidene)bicyclo[3.3.0]oct-1(2)-ene. To a solution of (*E*)-2-iodo-7-(5′-tetrahydropyranyloxypentylidene)bicyclo[3.3.0]oct-1(2)-en-3-one (1.35 g, 3.24 mmol) in 0.4 M $CeCl_3 \cdot 7\ H_2O$ [15] in MeOH (30 mL) was added $NaBH_4$ (160 mg, 4.23 mmol) at -20 °C. The mixture was warmed to 23 °C and evaporated. The residue was suspended in Et_2O and washed with brine, until the organic phase turned into a clear solution. The organic phase was dried over $MgSO_4$ and evaporated *in vacuo*. Chromatography of the residue on silica gel (30/70 Et_2O-hexane) afforded the title compound (1.19 g, 88%) as an oil: ^{1}H NMR ($CDCl_3$) δ 1.3-1.9 (m, 12 H), 1.9-2.05 (m, 2 H), 2.11 (dd, *J* = 6.6 and 1.9 Hz, 1 H), 2.65-2.9 (m, 5 H), 3.3-3.55 (m, 2 H), 3.65-3.95 (m, 2 H), 4.5-4.6 (m, 1 H), 4.8-5.0 (m, 1 H), 5.25-5.4 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.43, 25.33, 25.97, 28.87, 29.20, 30.57, 34.45, 36.50, 41.55, 48.72, 62.08, 67.31, 83.68, 91.96, 98.59, 123.65, 138.95, 158.22; IR (neat) 3418 (m) cm^{-1}; MS (m/z) 401 $(M+H-H_2O)^+$, 317, 275, 189, 85 (100).

(*E*)-2-Iodo-7-(5′-tetrahydropyranyloxypentylidene)-3-(trimethylsilyloxy)bicyclo-[3.3.0]oct-1(2)-ene (18). To a solution of (*E*)-3-hydroxy-2-iodo-7-(5′-tetrahydropyranyloxypentylidene)bicyclo[3.3.0]oct-1(2)-ene (1.15 g, 2.75 mmol) in CH_2Cl_2 (6 mL) was added Et_3N (580 μL, 4.16 mmol) and Me_3SiCl (450 μL, 3.55 mmol), and the reaction mixture was stirred at 23 °C for 14 h. The mixture was then diluted with Et_2O and washed with water. The organic phase was dried over Na_2SO_4 and evaporated to afford the title compound (1.29 g, 96%) as an oil: ^{1}H NMR (C_6D_6) δ 0.20 (s, 9 H), 1.15-1.85 (m, 12 H), 1.85-2.0 (m, 2. H), 2.2-2.35 (m, 1 H), 2.35-2.55 (m, 2 H), 2.6-2.8 (m, 1 H), 2.8-3.0 (m, 1 H), 3.25-3.5 (m, 2 H), 3.75-3.9 (m, 2 H), 4.60 (t, *J* = 3.4 Hz, 1 H), 4.65-4.8 (m, 1 H), 5.1-5.25 (m, 1 H).

2-[(*E*)-3′-(*t*-Butyldimethylsilyloxy)-1′-octen-1′-yl]-3-hydroxy-7-[(*E*)-5″-tetrahydropyranyloxypentylidene]bicyclo[3.3.0]oct-1(2)-ene (19). (a). Zincation of 18. To a solution of (*E*)-2-iodo-7-(5′-tetrahydropyranyloxypentylidene)-3-(trimethylsilyloxy)bicyclo-

[3.3.0]oct-1(2)-ene (760 mg, 1.55 mmol) in THF-Et_2O-pentane (4:1:1, 6 mL) was added 2.5 M *n*-BuLi (660 μL, 1.65 mmol) at -110 °C, and the reaction mixture was stirred at this temperature for 20 min. Dry $ZnBr_2$ (244 mg, 1.08 mmol) in THF (1 mL) was then added to the solution, and the resultant mixture was warmed to 23 °C. The solvents were subsequently removed under high vacuum, and the residue was redissolved in dry DMF (4 mL). **(b) Preparation of a Solution of 9 and the Pd Catalyst.** To a slurry of $Cl_2Pd[P(2\text{-furyl})_3]_2$ (50 mg, 0.08 mmol) in THF (0.8 mL) was added 2.5M *n*-BuLi (65 μL, 0.16 mmol) at -78 °C, and the reaction mixture was stirred at this temperature for 1 h. (*E*)-3-(*t*-Butyldimethylsilyloxy)-1-iodo-1-octene (743 mg, 2.02 mmol) in DMF (2 mL) was then added to the mixture, and the resultant mixture was warmed to 23 °C. **(c) Cross Coupling and Hydrolysis.** The solution of the organozinc derivative was added to the solution of the iodoalkene and the catalyst, and the resultant mixture was stirred at 23 °C for 2 h. The mixture was then diluted with Et_2O and washed with water. The organic phase was dried over Na_2SO_4 and evaporated. Analysis by NMR of the crude reaction mixture revealed the presence of the cross-coupling product in 90% yield. The crude mixture was dissolved in MeOH (10 mL), and K_2CO_3 (64 mg, 0.46 mmol) was added. After the reaction mixture was stirred at 23 °C for 30 min, it was diluted with Et_2O and washed with brine. The organic phase was dried over Na_2SO_4 and evaporated. Chromatography of the residue on silica gel (30/70 Et_2O-hexane) afforded the title compound (693 mg, 84%) as a mixture of diastereomers: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.0-0.1 (m with peaks at 0.028, 0.035, and 0.05, 6 H), 0.89 (t, J = 7 Hz, 3 H), 0.90 (s, 9 H), 1.2-1.9 (m, 21 H), 1.9-2.1 (m, 2 H), 2.6-2.85 (m, 3 H), 2.85-3.15 (m, 2 H), 3.3-3.4 (m, 1 H), 3.4-3.55 (m, 1 H), 3.65-3.8 (m, 1 H), 3.8-3.9 (m, 1 H), 4.1-4.2 (m, 1 H), 4.5-4.6 (m, 1 H), 5.05-5.25 (m, 1 H), 5.25-5.45 (m, 1H), 5.85-6.0 (m, 1 H), 6.14 (d, J = 16 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -4.80 (2), -4.26 (2), 13.99 (2), 18.19 (2), 19.51 (2), 22.52 (2), 24.90 (2), 25.40 (2), 25.85 (6), 26.10 (2), 28.96 (2), 29.28 (2), 30.64 (2), 31.77 (2), 31.85 (2), 35.94, 35.99, 38.43 (2), 42.87 (2), 46.65 (2), 62.11 (2), 67.39 (2), 73.47, 73.76, 81.46, 81.51, 98.65 (2), 121.22 (2), 122.88 (2), 130.93 (2), 134.01, 134.17, 141.54 (2), 149.99, 150.08; IR (neat) 3442 cm^{-1}; High resolution MS calcd for $C_{32}H_{56}O_4Si(+H-H_2O)$ 515.3921, found 515.3905. The ^{13}C NMR spectral data are presented for a 1:1 mixture of two diastereomers, in which five carbons show two discrete signals for the diastereomers.

2-[(*E*)-3′-(*t*-Butyldimethylilyloxy)-1′-octen-1′-yl]-7-[(*E*)-5″-(tetrahydropyranyloxy)pentylidene]bicyco[3.3.0]oct-1(2)-en-3-one (6b). To a solution of **19** (650 mg, 1.22 mmol) in CH_2Cl_2 (20 mL) was added pyridinium chlorochromate (790 mg, 3.66 mmol), and NaOAc (300 mg, 3.66 mmol). The reaction mixture was stirred at 23 °C for 2 h, diluted with Et_2O, and washed with water. The organic phase was dried over Na_2SO_4 and evaporated. Chromatography of the residue on silica gel (30/70 Et_2O-hexane) afforded the title compound (505 mg, 78%) as an oil: ^1H NMR (C_6D_6) δ 0.1-0.2 (m, 6 H), 0.8-0.95 (m, 3 H), 1.0-1.1 (m, 9 H), 1.1-1.8 (m, 20 H), 1.8-2.0 (m, 2 H), 2.15-2.45 (m, 3 H), 2.85 (d, J = 22.0 Hz, 1 H), 3.18 (dd, J = 22.0 and

12.4 Hz, 1 H), 3.3-3.5 (m, 2 H), 3.75-3.95 (m, 2 H), 4.2-4.35 (m, 1 H), 4.55-4.65 (m, 1 H), 5.1-5.3 (m, 1 H), 6.52 (d, J = 15.9 Hz, 1 H), 6.85-7.05 (m, 1 H); ^{13}C NMR (C_6D_6) δ -4.57, -4.04, -4.00, 14.27, 18.49, 19.74, 22.98, 25.33, 25.95, 26.15 (3C), 26.63, 29.38, 29.85, 31.08, 32.22, 33.86, 34.94, 38.80, 38.85, 42.69, 42.73, 42.89, 61.69, 67.33, 73.87, 74.05, 98.68, 118.39, 124.34, 131.59, 138.41, 138.47, 139.24, 179.12, 206.47; IR (neat) 1706 (s), 1646 (m), 1618 (m). Anal. calcd for $C_{32}H_{54}O_4Si$: C, 72.40; H, 10.25. Found: C, 72.22; H. 10.16.

2-[(*E*)-3′-(*t*-Butyldimethylsilyloxy)-1′-octen-1′-yl]-7-[(*E*)-5″-(tetrahydropyranyloxy)-pentylidene]bicyclo[3.3.0]octan-3-one (21). (a) Preparation of the Reagent [17]. Methanol (110 μL, 2.72 mol) in THF (1 mL) was added to 1 M $LiAlH_4$ in THF (0.91 mL, 0.91 mmol) at 0 °C. The solution was warmed to 23 °C, stirred for 30 min at this temperature, and then added to a suspension of freshly purified CuBr (65 mg, 0.45 mmol) in THF (1 mL) at -5 °C. The resultant mixture was vigorously stirred for 30 min while maintaining temperature within -5~0 °C. **(b) Conjugate Reduction.** 2-[(*E*)-3′-(*t*-Butyldimethylsilyloxy)-1′-octen-1′-yl]-7-[(*E*)-5″-(tetrahydropyranyloxy)pentylidene]bicyclo[3.3.0]oct-1(2)-en-3-one (120 mg, 0.23 mmol) in THF (2 mL) was added to the reagent prepared above at -78 °C, and the reaction mixture was stirred at this temperature for 10 min. The temperature was raised to -25 °C over 2 h. The reaction mixture was cooled to -40 °C, and MeOH (0.6 mL, 14.8 mmol) was added. The resultant slurry was warmed to 23 °C, diluted with Et_2O, and washed with saturated aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4 and evaporated. Analysis by ^{1}H NMR of the crude reaction mixture revealed the presence of the title compound formed in 38% NMR yield and the carbonyl reduction product **19** (33%). Chromatography of the residue on silica gel (85/15 hexane/Et_2O) afforded, in addition to a 28% (34 mg) of **19**, the title compound (40 mg, 33%) as a nearly 1:1 mixture of two diastereomers: ^{1}H NMR (C_6D_6) δ 0.12 (s, 3 H), 0.14 (s, 3 H), 0.15 (s, 3 H), 0.18 (s, 3 H), 0.89 (t, J = 6.9 Hz, 6 H), 1.02 (s, 9 H), 1.03 (s, 9 H), 1.1-2.0 (m, 40 H), 2.0-2.5 (m, 18 H), 3.25-3.5 (m, 4 H), 3.75-3.9 (m, 4 H), 4.05-4.2 (m, 2 H), 4.55-4.65 (m, 2 H), 5.2-5.3 (m, 2 H), 5.45-5.6 (m, 4 H); ^{13}C NMR (C_6D_6) δ -4.59, -4.54, -3.82 (2C), 14.25 (2C), 18.43 (2C), 19.72 (2C), 23.03 (2C), 25.43 (2C), 25.96 (2C), 26.18 (6C), 26.72 (2C), 29.85 (2C), 29.94 (2C), 31.10 (2C), 32.16 (2C), 34.97 (2C), 37.70 (2C), 38.13, 38.16, 38.80 (2C), 43.40, 43.45, 46.19, 46.39, 55.50, 55.64, 61.68 (2C), 67.39 (2C), 73.93, 74.06, 98.70 (2C), 123.36 (2C), 126.21, 126.36, 136.76, 137.10, 141.30 (2C), 215.47, 215.59; IR (neat) 2930, 1654 cm^{-1}. The ^{1}H and ^{13}C NMR spectral data are presented for a 1:1 mixture of two diastereomers.

3-(*t*-Butyldimethysilyloxy)-2-[(*E*)-3′-(*t*-butyldimethylsilyloxy)-1′-octen-1′-yl]-7-[(*E*)-5″-(tetrahydropyranyloxy)pentylidene]bicyclo[3.3.0]octane (15). To a solution of 2-[(*E*)-3′-(*t*-butyldimethylsiloxy)-1′-octen-1′-yl]-7-[(*E*)-5″-(tetrahydropyranyloxy)pentyliden]bicyclo-[3.3.0]octan-3-one (37 mg, 69.5 μmol) in MeOH (3 mL) was added $NaBH_4$ (5.3 mg, 140 μmol) at -30 °C. The reaction mixture was warmed up to 20 °C over 1 h. After removal of the solvent *in vacuo*, the residue was treated with brine, extracted with EtOAc, and dried (Na_2SO_4). After concentration *in vacuo*, the crude product **22** thus obtained was used in the following reaction without purification. A solution of the crude alcohol obtained as above, *t*-butyldimethylsilyl chloride (22 mg, 150 μmol), and imidazole (13.6 mg, 200 μmol) in DMF (3 mL) was stirred at 20 °C for 24 h. The reaction mixture was diluted with water (15 mL), extracted with diethyl eether, dried (Na_2SO_4), and concentrated *in vacuo*. Chromatography on silica gel (7/3 hexane-Et_2O) afforded the title compound (42 mg, 93%) as a colorless oil: ^{1}H NMR (C_6D_6) δ 0.05-0.2 (m, 12 H), 0.91 (t, J = 6.8 Hz, 3 H), 0.99 (s, 9 H), 1.05 (s, 9 H), 1.1-1.9 (m, 20 H), 2.0-2.5 (m, 9 H), 3.2-3.3 (m, 2H), 3.6-3.9 (m, 3 H), 4.1-4.2 (m, 1 H), 4.55-4.65 (m, 1 H), 5.25-5.4 (m, 1 H), 5.4-5.7 (m, 2 H); ^{13}C NMR (C_6D_6) δ -4.52, -4.38 (2C), -4.28, -4.16, -4.10, -3.83, -3.65, 14.29 (2C), 18.30 (2C), 18.50 (2C), 19.65 (2C), 23.08 (2C), 25.34, 25.62, 26.00 (2C), 26.15 (6C), 26.21 (6C), 27.07 (2C), 29.69 (2C), 29.89 (2C), 31.09 (2C), 32.29 (2C), 36.17, 36.35, 38.19 (2C), 38.62, 38.87, 38.99, 39.22, 43.07 (2C), 45.01, 45.28, 56.68, 57.04, 61.50 (2C), 67.39 (2C), 73.56, 74.38, 78.50, 78.71, 98.54 (2C), 122.23, 122.32, 131.47, 132.24, 134.82, 135.41, 141.89, 142.03; IR (neat) 2954, 2930, 1472, 1254, 1120, 1076, 1036, 970, 836, 774 cm^{-1}; High resolution MS (FAB) calcd for $C_{38}H_{72}O_4Si_2$ (-H) 647.4891, found 647.4871. The ^{13}C NMR signals are for two diastereomers. The NMR spectral data are in agreement with the published data [3b].

(*E*)-2-[3′-(*t*-Butyldimethylsilyloxy)-1′-octen-1′-yl]bicyclo[3.3.0]oct-1(2)-en-3-one (11). This compound was prepared in 72% yield as briefly reported in a previously published paper [4b] from **12** and **13** using 5 mol % of $Cl_2Pd(TFP)_2$ and 10 mol % of *n*-BuLi: ^{1}H NMR ($CDCl_3$, C_6H_6) δ -0.03 (s, 3 H), -0.02 (s, 3 H), 0.75-0.85 (m, 3 H), 0.82 (and 0.83) (s, 9 H), 1.1-1.3 (m, 6 H), 2.0-2.1 (m, 2 H), 1.9-2.15 (m, 5 H), 2.4-2.55 (m, 3 H), 2.7-2.8 (m, 1 H), 4.1-4.2 (m, 1 H), 6.1-6.2 (m, 1 H), 6.25-6.4 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ -4.84, -4.39, -4.33, 13.94, 18.16, 22.50, 24.82, 25.82, 26.12, 26.29, 31.18, 31.74, 38.25, 38.31, 42.10, 44.62, 73.48, 73.61, 117.55, 117.61, 131.52, 137.91, 137.97, 183.75, 183.79, 203.72; IR (neat) 1708 (s), 1642 (w), 1620 (w), 1255 (m), 980 (m), 840 (s), 780 (m) cm^{-1}; High resolution MS calcd for $C_{22}H_{38}O_2Si$ 362.2641, found 362.2640. The NMR spectral data listed above correspond to a 1:1 mixture of two diastereomers.

(*E*)-2-[3′-(*t*-Butyldimethylsilyloxy)-1′-octen-1′-yl]-3-hydroxybicyclo[3.3.0]oct-1(2)-ene (17). This compound was prepared from **16** in a manner similar to the preparation of **19** in 65% yield: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.03 (s, 3 H), 0.05 (s, 3 H), 0.86 (t, J = 6 Hz, 3 H), 0.90 (s, 9 H), 1.0-2.1 (m, 14 H), 2.15-2.4 (m, 2 H), 2.5-2.7 (m, 2 H), 4.1-4.2 (m, 1 H), 5.1-5.25 (m, 1 H), 5.8-5.95 (m, 1 H), 6.14 (d, J = 16 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -4.73, -4.22, 14.04, 18.26, 22.59, 23.54, 25.00, 25.90 (3C), 27.47, 31.83, 32.27, 38.52 (and 38.57), 42.13, 48.32, 73.64 (and 73.86), 82.71 (and 82.77), 121.51 (and 121.55), 130.38, 133.60 (and 133.71), 153.12 (and 153.22). Anal. calcd for $C_{22}H_{40}O_2Si$: C, 72.46; H, 11.06. Found: C, 72.74; H, 10.77.

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