Intramolecular Metallo–Ene–Allene Reactions. A New Carbocycles Synthesis

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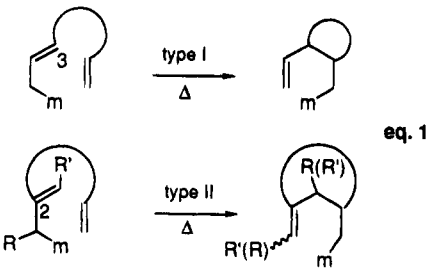
Polysubstituted enynes have been lithiated on the propargylic position, and transmetalation to the corresponding zinc reagents promotes an easy cyclization reaction leading to polysubstituted cyclopentylmethylzinc derivatives. This cyclization is stereospecific, and a single diastereoisomer is formed, even when a tertiary and a quaternary center are linked in the process. The reaction is considered to take place *via* a metallo–ene–allene process.

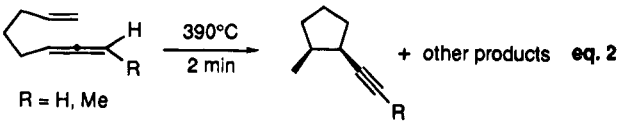
Introduction

Additions of allylmetal compounds to alkenes and alkynes are considered as metallo–ene reactions.[1] Problems of low regio- and stereoselectivity and low overall efficiency may limit the applicability of the addition of allylzinc,[2] -magnesium,[3] -lithium,[4] -aluminum,[5] -boron,[6] -palladium,[7] and -nickel[8] reagents to alkenes, acetylenes, allenes, and enol ethers in bimolecular reactions. In contrast, intramolecular metallo–ene reactions, entropically favored, represent a powerful methodology for the construction of polysubstituted cycloalkanes. Two different modes of cyclization have been described in which the enophile is linked by a suitable bridge, either to the terminal carbon atom (C-3, type I) or to the central carbon atom (C-2, type II) of the metallo–ene unit (eq 1)[1].

Among the various studies on the carbocyclization of organometallics of 5-hexenyl type,[9] we have shown, for the first time, the propensity of functionalized primary[10] and secondary[11] organozinc reagents to cyclize via an anionic pathway. In the case where such a secondary zinc reagent would be of propargylic nature, it became interesting to investigate a plausible metallo–ene–allene reaction.

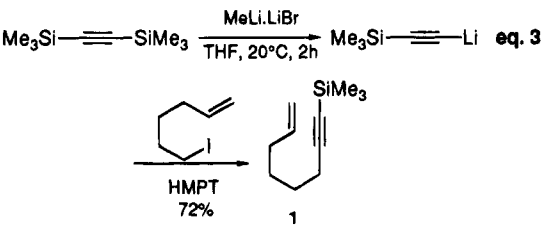
Although the ene–allene reaction was disclosed by Huntsmann 10 years ago[12] to interpret the formation of a cyclic product by pyrolysis of 2,3,8-nonatriene and 1,2,7-octatriene (eq 2), the metallo–ene-allene reaction has never received attention in organic synthesis.





Results and Discussion

8-(Trimethylsilyl)-1-octen-7-yne (**1**) was first synthesized via alkylation of 6-iodo-1-hexene with [(trimethylsilyl)ethynyl]lithium[13] in 72% yield (eq 3).



1 was cleanly metalated with s-BuLi in THF at −45 °C or in Et_2O at +10 °C. However, upon standing for

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1995.

(1) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38. (b) Oppolzer, W. *Comprehensive Organic Synthesis*; Trost, B., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 5, p 28. (c) Van der Louw, J.; Van der Baan, J. L.; Stieltjes, H.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1987**, *28*, 3083.

(2) (a) Lehmkuhl, H.; Nehl, H. *J. Organomet. Chem.* **1973**, *60*, 1. (b) Frangin, Y.; Gaudemar, M. *Bull. Soc. Chim. Fr.* **1976**, 1173. (c) Bernadou, F.; Miginiac, L. *Tetrahedron Lett.* **1976**, 3083. (d) Negishi, E. I.; Miller, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6761. (e) Molander, G. A. *J. Org. Chem.* **1983**, *48*, 4509.

(3) (a) Felkin, H.; Umpleby, J. D.; Hagaman, E.; Wenkert, E. *Tetrahedron Lett.* **1972**, 2285. (b) Felkin, H.; Kwart, L. D.; Swierczewski, G.; Umpleby, J. D. *J. Chem. Soc., Chem. Commun.* **1975**, 242. (c) Fukutani, H.; Takizawa, M.; Okada, H. Jpn. Pat. 1972, 034, 7239; *Chem. Abstr.* **1973**, *78*, 111498.

(4) Josey, A. D. *J. Org. Chem.* **1974**, *39*, 139.

(5) Stefani, A. *Helv. Chim. Acta* **1973**, *56*, 1192.

(6) (a) Mikhailov, B. M.; Yu, N.; Bubnov, O. *Tetrahedron Lett.* **1971**, 2127. (b) Yu, N.; Bubnov, O.; Nesmeyanova, T.; Rudashevskaya, Y.; Mikhailov, B.M. *Tetrahedron Lett.* **1971**, 2153.

(7) (a) Takahashi,T.; Sakai, S.; Ishii, Y. *J. Organomet. Chem.* **1969**, *16*, 177. (b) Kiji, J.; Miura, Y.; Furukawa, J. *J. Organomet. Chem.* **1977**, *140*, 317. (c) Larock, R. C.; Burkhart, J. P.; Oertle, K. *Tetrahedron Lett.* **1982**, *23*, 1071.

(8) (a) Gallazi, M. C.; Hanton, T. L.; Vitulli, G.; Porri, L. *J. Organomet. Chem.* **1971**, *33*, C45. (b) Gattelani, M.; Chiusoli, G. P.; Dradi, E.; Salerno, G. *J. Organomet. Chem.* **1977**, *177*, C29.

(9) (a) Hill, A. E. *J. Organomet. Chem.* **1975**, *71*, 123. (b) Saint Denis, J.; Dolzine, T.; Oliver, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 8260. (c) Smith, M. J.; Wilson, S. *Tetrahedron Lett.* **1981**, *22*, 4615. (d) Bajgrowicz, J. A.; Hallaoui, A. E.; Jacquier, R.; Pigrese, C.; Viallefont, P. *Tetrahedron* **1985**, *41*, 1833. (e) Ashby, E. C.; Pham, T. N. *J. Org. Chem.* **1987**, *52*, 1291. (f) Dolbier, W. R., Jr.; Chen, Y. *J. Org. Chem.* **1992**, *57*, 1947. (g) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K. V. *J. Am. Chem. Soc.* **1992**, *114*, 8053. (h) Bailey, W. F.; Zarcona, L. M. J. *Tetrahedron Lett.* **1991**, *32*, 4425. (i) Bailey, W. F.; Khanolkar, A. T.; Gavaskar, K. V.; Ovaska, T. V.; Rossi, K.; Thiel, Y.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 5720. (j) Krief, A.; Derouare, D.; Dumont, W. *Synlett* **1992**, 907. (k) Krief, A.; Barbeaux, P. *Tetrahedron Lett.* **1991**, *32*, 417. (l) Krief, A.; Barbeaux, P. *Synlett* **1990**, 511. (m) Chamberlain, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788. (n) Mudryl, B.; Cohen, T. *J. Am. Chem. Soc.* **1993**, *115*, 3855. (o) Broka, C. A.; Shen, T. *J. Am. Chem. Soc.* **1989**, *111*, 2981. (p) Young, J. R.; Stille, J. R. *J. Am. Chem. Soc.* **1992**, *114*, 4936.

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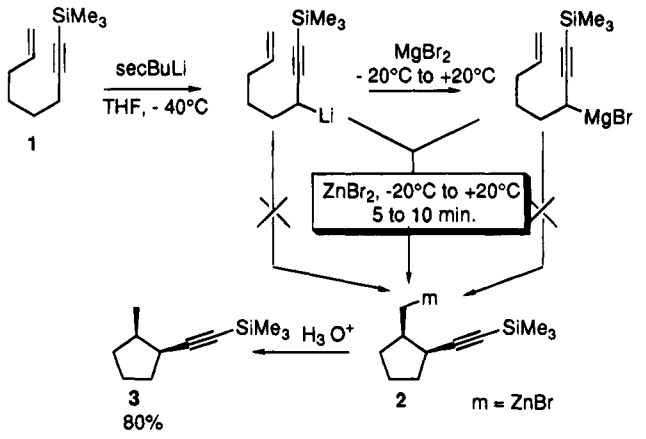
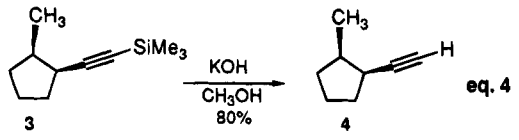
Scheme 1



1–2 h at 20 °C, no cyclization of the corresponding organolithium reagent was observed since hydrolysis of the reaction mixture produced the starting enyne and its allenic counterpart in a 60/40 ratio. Addition of 1 equiv of magnesium salt to the lithium derivative did not lead to the cyclic product either (the propargyl/allenyl ratio then became 67/33). However, addition of 1 equiv of $ZnBr_2$ at −20 °C not only modified the propargyl/allenyl ratio[14] of the hydrocarbons arising from protonation of the organometallic species at low temperature (propargyl/allenyl 98/2) but also resulted in a virtually quantitative cyclization reaction after stirring for *a few minutes* at room temperature (Scheme 1).

Hydrolysis of the reaction mixture afforded **3** in 80% yield as a single diastereoisomer. The *cis* stereochemistry was determined by comparison of the known ^{13}C NMR spectra of both isomers[12,15] with that of the desilylated cyclic derivative **4** (eq 4):

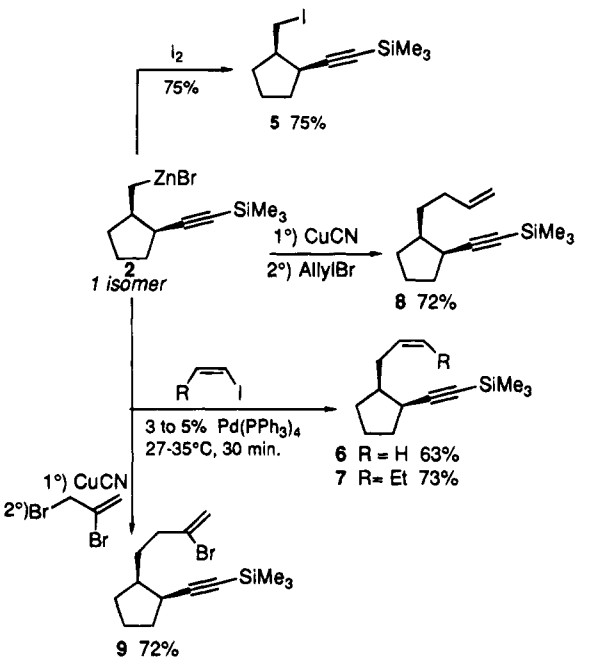


eq. 4

The formation of a discrete organometallic species was checked by iodinolysis, by coupling reactions with vinylic iodides in the presence of a catalytic amount of $Pd(PPh_3)_4$, or by reaction with allylic halides after transmetalation of the organozinc bromide into an organocopper reagent[16] (Scheme 2).

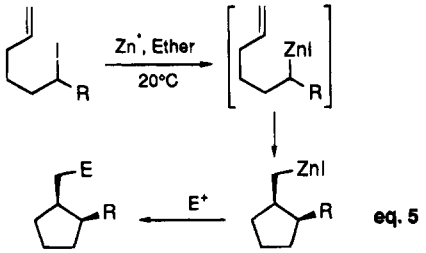
According to this scheme, some new cyclic 1,6- or 1,7-enynes could be generated as single isomers. Heating the solution of the cyclized organozinc bromide **2** in toluene at 120 °C did not produce the thermodynamic

Scheme 2



trans derivatives, indicating the nonreversibility of this cyclization.

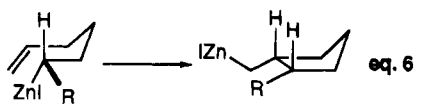
In our preceding study on the carbocyclization of ϵ-ethylenic secondary organozinc iodides,[11] we had shown that, contrary to their organolithium or organomagnesium analogues, the organozinc derivatives predominantly lead to the *cis*-1,2-disubstituted cyclopentanes, with a 75/25 *cis/trans* ratio (eq 5).



eq. 5

R = Me, Bu, iPr, terBu

In all these reactions, the *cis* stereoselectivity observed is attributed to steric interactions which favor a geometry in which the R substituent preferentially occupies an outside position in the chairlike transition state (eq 6).



eq. 6

Cis / *Trans* : 75 / 25

However, in the present case of metallated propargylic derivatives, *only* the *cis* diastereoisomer is obtained (Scheme 1). Comparison of the conformational free energy difference of the methyl and ethynyl groups located on the chair form of a cyclohexane[17] does not explain the discrepancy between the diastereoisomeric ratio (75/25 as in eq 6 versus single isomer as in Scheme 1). A more plausible explanation would be to consider a

(10) Meyer, C.; Marek, I.; Courtemanche, G.; Normant, J.-F. *Synlett* **1993**, 266.

(11) (a) Meyer, C.; Marek, I.; Courtemanche, G.; Normant, J.-F. *Tetrahedron Lett.* **1993**, *34*, 6053. (b) Meyer, C.; Marek, I.; Courtemanche, G.; Normant, J.-F. *Tetrahedron* **1994**, *50*, 11665–11692.

(12) Hunstmann, W. D.; Li, Y. J.; Giannamore, V. *Isr. J. Chem.* **1985**, *26*, 88.

(13) Holmes, A. B.; Jennings-White, C. L. D.; Schulthess, A. H.; Walton, D. R. M.; Akinde, B. *J. Chem. Soc., Chem. Commun.* **1979**, 840.

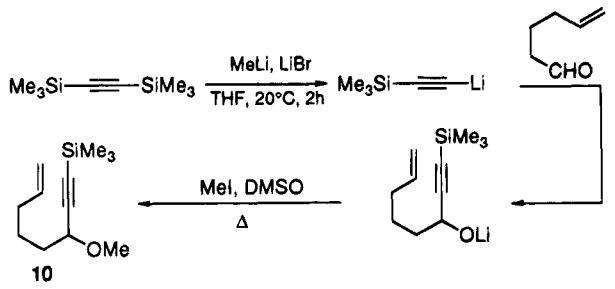
(14) This observation is clearly consistent with a transmetalation step from the organolithium to the organozinc derivatives.

(15) Brown, H. C.; Mahindroo, V. K.; Bhat, N. G. *J. Org. Chem.* **1991**, *56*, 1500.

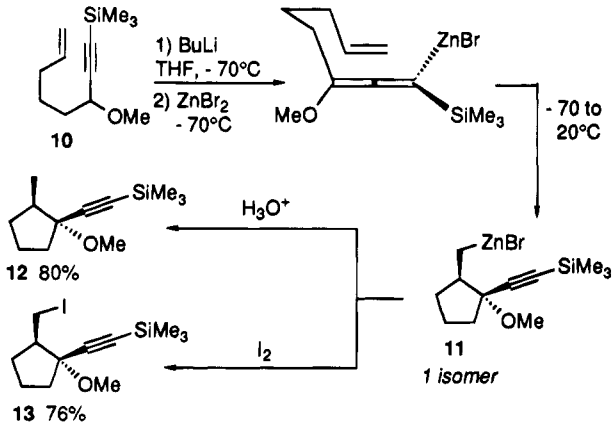
(16) For a review see: (a) Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, 23, 2117. (b) Knochel, P.; Rozema, M. J.; Tucker, C. E.; Retherford, C.; Furlong, M.; Achyatha Rao, S. *Pure Appl. Chem.* **1992**, 64, 361. (b) Achyatha Rao, S.; Knochel, P. *J. Org. Chem.* **1991**, 56, 4591.

(17) Booth, H.; Everett, J. R. *J. Chem. Soc., Chem. Commun.* **1976**, 278.

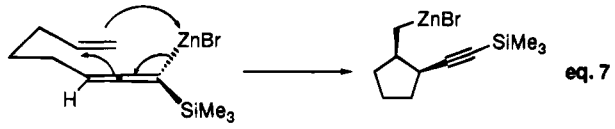
Scheme 3



Scheme 4



metallo–ene–allene reaction[18] in which the allenyl metal moiety plays the role of the ene moiety and fixes the *cis* relationship of the two substituents (eq 7).



eq. 7

In any case, the cyclization of the allenyl organozinc reagents proceed under very mild conditions (5–10 min at 20 °C) compared to the known metallo–ene reactions of allylic Grignard reagents (Mg powder, 60 °C, 24 h).[1] We thus decided to test the scope of this reaction for the stereoselective construction of polysubstituted five-membered carbocycles.

Propargylic Ether Derivatives. The starting material **10** was prepared, in a one pot procedure,[13,19] with an 81% yield according to Scheme 3.

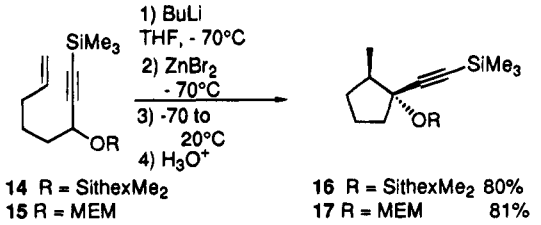
Metalation of the propargylic ether **10** with s-BuLi in THF at −70 °C followed by transmetalation with $ZnBr_2$ into the corresponding organozinc bromide resulted, upon warming to room temperature, in a highly diastereoselective cyclization reaction[18] (Scheme 4).

Hydrolysis of the reaction mixture afforded **12** in 80% yield as a single isomer. The presence of a metal in **11** was shown by iodinolysis to **13**. No traces of **12** were found after quenching the organometallic with this electrophile, a fact which confirms the stability of **11** toward adventitious protonation in THF at room temperature.

(18) Contrary to our initial report in which the C_{SP3} organozinc cyclization was postulated instead of the metallo–ene–allene mechanism: Courtemanche, G.; Normant, J. F. *Tetrahedron Lett.* **1991**, *32*, 5317.

(19) Van Run, P. E.; Mommers, S.; Visser, R. G.; Verkruijsse, H. D.; Brandsma, L. *Synthesis* **1981**, 459.

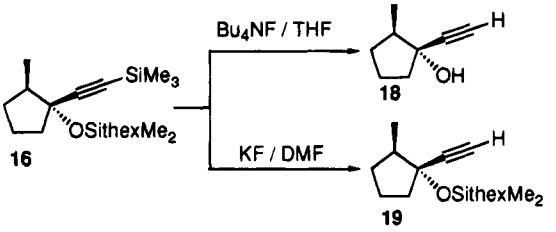
Scheme 5



14 R = SithexMe$_2$
15 R = MEM

16 R = SithexMe$_2$ 80%
17 R = MEM 81%

Scheme 6



In order to prepare the free alcohol corresponding to **12**, we devised the preparation of other ethers, known to cleave easily. The benzyl ether was not satisfactory since its metalation led instantaneously to a Wittig rearrangement,[20] but the thexyldimethylsilyl ether **14** or the methoxyethoxy methyl ether **15** undergo cyclization to give, respectively, after hydrolysis, **16** and **17** as *single isomers* (Scheme 5).

Interestingly, **16** can be selectively or totally desilylated, according to the fluoride used (respectively, potassium or tetrabutylammonium fluoride) as depicted in Scheme 6.

The stereochemical outcome of this carbocyclization was determined on **18** by comparison with the literature data[21ab] concerning both *cis* and *trans* isomers of this derivative and also by the preparation of the saturated analog of **18**[21c] which was identical to the *cis* isomers of 2-methyl-1-ethylcyclopentan-1-ol. The relative configuration of this single isomer is, again, difficult to rationalize by the transition state depicted in eq 6, since, according to what is accepted for the cyclization of the corresponding Csp^3–Zn[11] or Csp^3–metal,[9] the suprafacial addition of C–ZnBr on C=C would bring into competition two groups of bulky steric requirement. On the other hand, the metallo–ene–allene transition state (in which the alkoxy group occupies a definite allenic position, see Scheme 4) is in good agreement with the stereochemistry of the cyclized product. According to this finding, a quaternary and tertiary stereogenic center on a cyclopentane ring can be easily created with a total diastereoselection by a metallo–ene–allene reaction. In the following study, we extended the scope of this reaction to the creation of quaternary stereogenic centers without heteroatoms.

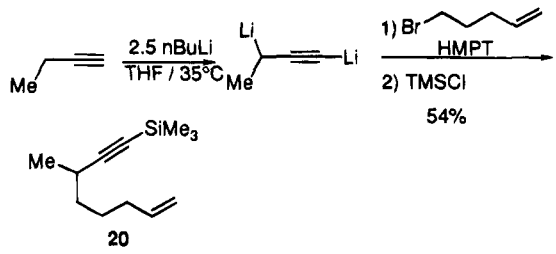
Substituted Propargylic Derivatives. Another interesting substituted enyne with an alkyl group in the propargylic position was studied. The starting material **20** was synthesized, in a one pot procedure, by dimetalation of butyne[22] followed sequentially by the introduc-

(20) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885 and references cited therein.

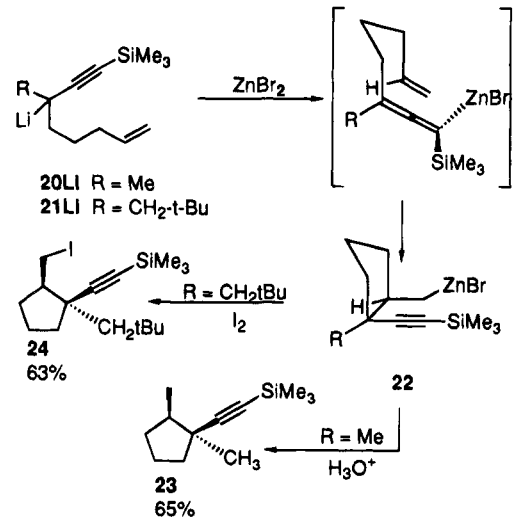
(21) (a) Battioni, J. P.; Capmau, M. L.; Chodkiewicz, W. *Bull. Soc. Chim. Fr.* **1969**, *3*, 976. (b) Battioni, J. P.; Chodkiewicz, W. *Bull. Soc. Chim. Fr.* **1969**, *3*, 981. (c) Cannone, P.; Bernatchez, M. *J. Org. Chem.* **1986**, *51*, 2147.

(22) Brandsma, L.; Verkruijsse, H. D. *Synthesis of acetylenes, allenes and cumulenes*; Elsevier: New York, 1981.

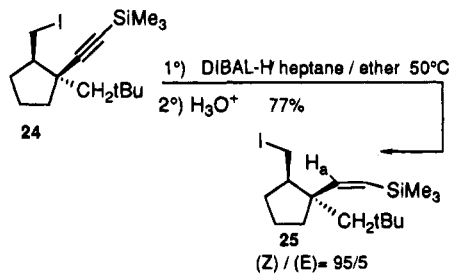
Scheme 7



Scheme 8



Scheme 9



tion of 1 equiv of 1-bromo-4-pentene and by 1 equiv of TMSCl leading to the silylated enyne in 54% yield (Scheme 7).

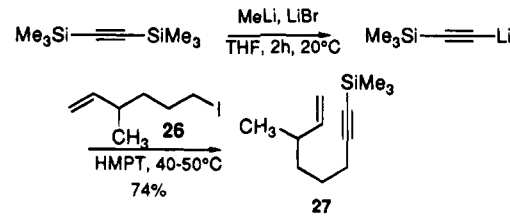
The metalation was carried out at 0 °C in THF for **20**, and for **21Li** the metalated enyne was synthesized according to the literature.[23] After transmetalation of **20Li** into the corresponding organozinc bromide, the latter undergoes a rapid and clean metallo–ene–allene reaction to give the corresponding cyclopentane with total diastereoselection (Scheme 8).

The creation of a cyclopentane bearing a methylene–metal unit and an adjacent quaternary center as a single diastereomer is thus readily available. In order to determine the stereochemistry of the new quaternary center, we have slightly modified the cyclopentane skeletton without altering the stereogenic centers, as described in Scheme 9.

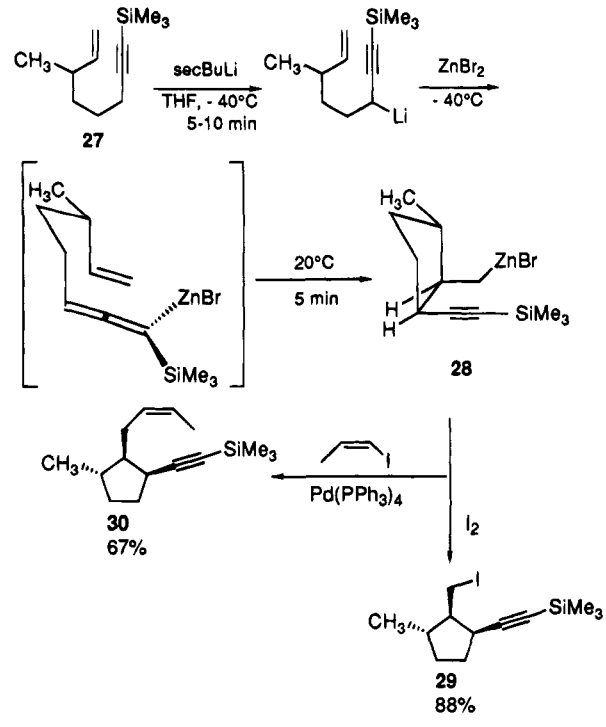
A strong nuclear Overhauser effect was observed between the protons of the iodomethyl group and H_a. Here again, the stereochemistry of the cyclic product was in full agreement with the metallo–ene–allene transition state.

(23) (a) Miginiac, L. *J. Organomet. Chem.* **1982**, *238*, 235. (b) Stadnichuk, M. D.; Petrov, A. A. *Zh. Obsh. Khim.* **1962**, *32*, 2490.

Scheme 10



Scheme 11



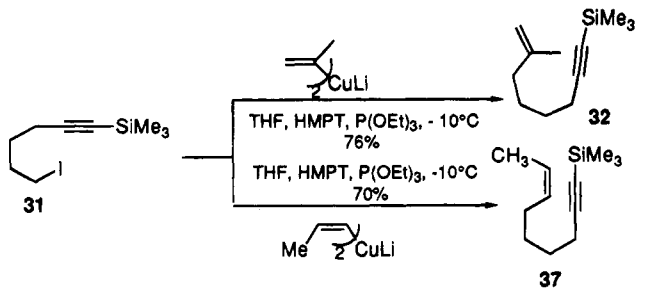
Substituted Allylic Derivatives. Finally, we turned our attention to the enynes in which the substituent is located on the allylic position. The enyne **27** was synthesized as described in Scheme 10, by alkylation of 6-iodo-3-methyl-1-hexene **26**[9] with [(trimethylsilyl)ethynyl]lithium in 74% yield (Scheme 10).

According to our "metalation–transmetalation" procedure, the allenyl organozinc bromide reagent undergoes a highly diastereoselective cyclization reaction (Scheme 11).

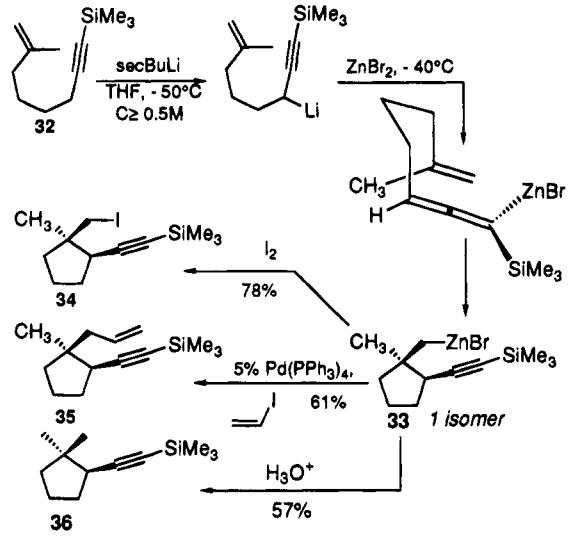
Quenching the resulting organometallic with iodine or coupling it with (*Z*)-1-iodo-1-propene afforded, respectively, **29** and **30** as *single isomers*. The ^1H and ^{13}C NMR chemical shifts of **29** were established by using standard COSY techniques, and unambiguous configurational assignments were found on the basis of diffencial nuclear Overhauser effect spectra. The relative configuration of **29** (1*S**,2*R**,3*S**) was easily attributed to steric interactions in the metallo–ene–allene transition state that favor a geometry in which the methyl substituent preferentially occupies a pseudoequatorial position. Thus, three contiguous stereogenic center on a cyclopentane ring have been easily created with a total diastereoselection.

Enynes with α,α and α,β Disubstituted Double Bonds. The following enynes **32** and **37** were respectively synthesized via alkylation of diisopropenyl and di-

Scheme 12



Scheme 13



(*Z*)-propenyl cuprates[24] with 1 equiv of 6-iodo-1-(trimethylsilyl)-1-hexyne (**31**) as described in Scheme 12.

Enyne **32** was subjected to our "metalation–transmetalation" procedure previously described. We found that the greater the initial concentration, the higher the cyclization yield. The maximal proportion of cyclic organozinc reagent was formed within 2–3 h at room temperature; this shows that disubstitution at the α carbon slows down the cyclization rate (Scheme 13).

The stereochemistry of **34** was assigned on the basis of differential NOE effects: Irradiation of the methyl group resulted in an enhancement of the signal intensity of the propargylic proton. This *single* exclusive relative stereochemistry can be easily explained by the metallo–ene–allene transition state. By this carbocyclization reaction, we are able to create a quaternary carbon which bears a methyl and a metalated methyl group diastereospecifically on a cyclopentane.

However, no cyclization was observed when enyne **37** with an α,β disubstituted double bond was subjected to an analogous metalation. This result represents the first limitation of this new carbocyclization: only the terminal olefinic enophile units insert into the allenylzinc bromide reagent.

Conclusion

The discovery of an effective metallo–ene–allene reaction from polysubstituted enynes represent a new and promising way to generate polysubstituted cyclopentyl methylzinc derivatives under very mild cyclization conditions: the requisite organometallic is easily prepared by low-temperature metalation of enynes followed by transmetalation into the organozinc bromide. On warming to room temperature, the propargylic (allenic) derivatives undergo a clean and totally regiospecific 5-*exo-trig* cyclization to give the cyclic product which can be elaborated with suitable electrophiles. We are currently investigating an extension of the work described above to the preparation of more complex systems, such as metallo–yne–allene reactions,[25] and natural products synthesis.

Experimental Section[11b]

Microanalyses were obtained from the University Pierre et Marie Curie laboratories.

8-(Trimethylsilyl)-1-octen-7-yne (1). A solution of bis(trimethylsilyl)acetylene (20.45 g, 0.12 mol) in dry THF (120 mL) was cooled to −30 °C as methyllithium (93.7 mL, 1.28 M in ether prepared from CH_3Br, 0.12 mol) was added rapidly. After the solution was stirred for 2 h at 20 °C, 6-iodo-1-hexene (21 g, 0.1 mol) was added followed by dry HMPA (25 mL), which caused the temperature to raise over 35 °C. The reaction mixture was stirred overnight at room temperature and was then poured into 3 M hydrochloric acid. It was extracted with ether, and the combined extracts were dried over $MgSO_4$. The solvents were evaporated and the residue purified by distillation under reduced pressure, bp = 80–82 °C (13 Torr), to give 12.6 g (70%) of the title compound **1** as a colorless liquid. IR (film): 2175, 1640, 1245, 1020, 990, 840, 755 cm^{-1}. ^1H NMR (200 MHz): δ 5.79 (ddt, *J* = 17.0, 10.3, 6.8 Hz, 1H), 5.02–4.89 (m, 2H), 2.05 (m, 4H), 1.5 (m, 4H), 0.13 (s, 9H). ^{13}C NMR (50 MHz): δ 136.7, 114.7, 107.6, 84.6, 33.4, 28.2, 19.9, 0.35. Anal. Calcd for $C_{11}H_{20}Si$: C, 73.25; H, 11.18. Found: C, 73.37; H, 11.28.

Typical Procedure for the Cyclization of Propargylic Organozinc Reagents. A solution of the enyne in dry THF or ether (10–15 mL) was cooled to −40 °C (in THF) or 10 °C (in ether) as *sec*-butyllithium (1.3 M in cyclohexane/hexane = 92/8, 1.1–1.3 equiv) was added dropwise. The color of the solution immediately turned to yellow-orange. The efficiency of the metalation process can be monitored by GC as follows:

A hydrolyzed aliquot (1 M HCl) was analyzed by GC, indicating the presence of the starting material and its allenic counterpart (ratios ranging from 40/60 at −40 °C to 60/40 at 0–20 °C).

Another aliquot was quenched with freshly distilled pivalaldehyde or trimethylchlorosilane, followed by hydrolysis. GCanalysis indicated that no starting material was left.

When the metalation has reached completion, zinc bromide (1 M in ether, 1 to 1.3 equiv) was added dropwise at −30 °C, and the reaction mixture was allowed to warm to room temperature and stirred for a further 10–15 min. The reaction mixture was cooled to −5 °C as 1 M hydrochloric acid (10 mL) was added slowly. Ether was added, and the layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$ and stirred for at least 3 h with a few $Na_2S{\cdot}9H_2O$ crystals that enabled the removal of all zinc salts before further purification (otherwise isolated yields are lower than those reported). These were then removed by filtration, and the organic solution was washed with brine, dried over $MgSO_4$ and concentrated.

***cis*-2-Methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (3).** Enyne **1** (360 mg, 2 mmol) was subjected to both cyclization in THF and hydrolysis procedures as described above in the typical procedure. The crude product was purified by flash chromatography (eluent, pentane) to give 288 mg (80%) of the title compound **3** as a colorless liquid. IR (film): 2950, 2820, 2150, 1455, 1240, 835, 755 cm^{-1}. ^1H NMR (400 MHz): δ 2.70 (m, 1H), 2.02 (m, 1H), 1.86 (m, 1H), 1.73 (m, 3H), 1.52 (m, 1H), 1.34 (m, 1H), 1.03 (d, *J* = 6.60 Hz, 3H), 0.14 (s, 9H). ^{13}C NMR (50 MHz): δ 109.7, 86.2, 37.7, 36.8,

(24) Normant, J. F.; Alexakis, A.; Cahiez, G. *Tetrahedron Lett.* **1980**, *32*, 935.

(25) For a preliminary result see: Meyer, C.; Marek, I.; Normant, J. F. *Tetrahedron Lett.* **1994**, *35*, 5645.

32.8, 23.4, 16.9, 0.45. Anal. Calcd for $C_{11}H_{20}Si$: C, 73.25; H, 11.18. Found: C, 73.15; H, 11.30.

***cis*-1-Ethynyl-2-methylcyclopentane (4).** To a solution of **3** (200 mg, 1.11 mmol) in methanol (2 mL) was added potassium hydroxide (0.5 mL, 3 M in water, 1.5 mmol). The reaction mixture was stirred for 24 h at room temperature. It was then diluted with water (10 mL) and extracted with pentane (3 × 15 mL). The combined extracts were dried over K_2CO_3, and the solvents were distilled off to give 103 mg (80%) of the title compound **4** as a colorless liquid that was not further purified. ^{1}H NMR (200 MHz): δ 2.7 (m, 1H), 2.04 (d, J = 2.82 Hz, 1H), 2.00–1.13 (m, 7H), 1.07 (d, J = 6.84 Hz, 3H). ^{13}C NMR (50 MHz): δ 86.6, 70.1, 37.6, 35.6, 32.6, 29.8, 23.2, 16.7.

***cis*-2-(Iodomethyl)-1-[(trimethylsilyl)ethynyl]cyclopentane (5).** Enyne **1** (360 mg, 2 mmol) was subjected to the cyclization procedure in THF, and then the reaction mixture was cooled with an ice–water bath as an excess of solid iodine (2–3 equiv) was added. After the mixture was stirred for 10 min at room temperature, 1 M hydrochloric acid (10 mL) and ether (10 mL) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$ and dilute $Na_2S_2O_3$. They were then stirred for at least 3 h with a few $Na_2S{\cdot}9H_2O$ crystals. The solid was then removed by filtration, and the organic solution was washed with brine, dried over $MgSO_4$, and concentrated. The crude material was purified by flash chromatography (eluent, pentane) to give 460 mg (75%) of the title compound **5** as a pale yellow oil. ^{1}H NMR (400 MHz): δ 3.40 (A part of ABX, J_{AB} = 9.35 Hz, J_{AX} = 7.15 Hz, 1H), 3.22 (B part of ABX, J_{AB} = 9.35 Hz, J_{BX} = 8.25 Hz, 1H), 2.93 (m, 1H), 2.31 (X part of ABX, 1H), 2.00–1.8 (m, 4H), 1.63 (m, 1H), 1.45 (m, 1H), 0.13 (s, 9H). ^{13}C NMR (50 MHz): δ 107.0, 87.9, 46.8, 36.5, 33.2, 31.5, 23.6, 8.95, 0.38. Anal. Calcd for $C_{11}H_{19}SiI$: C, 43.14; H, 6.25. Found: C, 43.38; H, 6.18.

***cis*-2-(2-Propenyl)-1-[(trimethylsilyl)ethynyl]cyclopentane (6).** A solution of iodine (8.37 g, 33 mmol) in dry THF (12 mL) was cooled to −30 °C as vinylmagnesium chloride (15.6 mL, 2.3 M in THF, 36 mmol) was added dropwise. After the solution was stirred for 5 min at room temperature, $Pd(PPh_3)_4$ (692 mg, 0.6 mmol) was added and the resultant mixture was transferred via cannula into a solution of the cyclic organozinc reagent in THF prepared according to the general procedure from enyne **1** (3.6 g, 20 mmol). An exothermic reaction started, and the temperature of the reaction mixture rose to 30 °C. Heating was further maintained at 28–30 °C for 30 min. The reaction mixture was then hydrolyzed and worked up as for the typical procedure. The crude material was dissolved in pentane (80 mL), and the catalyst was removed by filtration through a pad of Celite. The solvent was evaporated and the crude product purified by distillation under reduced pressure, bp = 66–69 °C (0.5 Torr), to give 2.59 g (63%) of the title compound **6** as a colorless oil. IR (film): 3060, 2960, 2860, 2155, 1640, 1445, 1245, 990, 905, 830, 755 cm^{-1}. ^{1}H NMR (400 MHz): δ 5.83 (ddt, J = 17.05, 10.45, 7.15 Hz, 1H), 5.04 (d, J = 17.05 Hz, 1H), 4.97 (d, J = 10.45 Hz, 1H), 2.81–2.69 (m, 1H), 2.40–2.33 (m, 1H), 2.12–1.89 (m, 1H), 1.86–1.66 (m, 4H), 1.55 (m, 2H), 1.42–1.37 (m, 1H), 0.14 (s, 9H). ^{13}C NMR (100 MHz): δ 138.3, 115.3, 109.1, 86.8, 43.5, 35.5, 36.7, 32.9, 30.1, 23.1, 0.43. Anal. Calcd for $C_{13}H_{22}Si$: C, 75.65; H, 10.74. Found: C, 75.42; H, 10.93.

(*Z*)-*cis*-2-(2-Pentenyl)-1-[(trimethylsilyl)ethynyl]cyclopentane (7). Enyne **1** (2 g, 11.1 mmol) was subjected to the cyclization procedure in THF. A solution of (*Z*)-1-iodo-1-butene (2.26 g, 1.3 equiv) and $Pd(PPh_3)_4$ (641 mg, 0.55 mmol) in dry THF (5 mL) was added at room temperature, and the resultant mixture was immediately warmed at 28–30 °C for 30 min. It was then hydrolyzed and worked up as described for the typical procedure. The crude material was purified by flash chromatography (eluent, pentane) to give 1.89 g (73%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz): δ 5.36 (m, 2H), 2.76 (m, 1H), 2.29 (m, 2H), 2.08 (m, 2H), 1.89–1.34 (m, 7H), 0.97 (t, J = 7.7 Hz, 3H), 0.15 (s, 9H). ^{13}C NMR (50 MHz): δ 132.2, 128.5, 109.3, 44.3, 35.7, 32.9, 30.1, 29.4, 23.0, 20.8, 14.5, 0.40.

***cis*-2-(3-Butenyl)-1-[(trimethylsilyl)ethynyl]cyclopentane (8).** Enyne **1** (2 g, 11.1 mmol) was subjected to the cyclization procedure in THF. CuCN·2LiCl (11.6 mL, 1 M in THF, 11.6 mmol) was subsequently added. The greenish solution of the corresponding organozinc copper reagent was stirred for 10 min at 0 °C. It was then cooled to −40 °C, as freshly distilled allyl bromide (1.6 g, 13 mmol) was added via syringe. The reaction mixture was slowly allowed to warm to room temperature overnight, and it was then quenched with a saturated NH_4Cl 32%/NH_4OH 2/1 solution. After usual workup, the crude material was purified by flash chromatography (eluent, pentane) to give 1.75 g (72%) of the title compound **8** as a colorless oil. ^{1}H NMR (400 MHz): δ 5.86 (m, 1H), 5 (dd, 2H, J = 17.05, 9.9 Hz), 2.8 (m, 1H), 2 (m, 2H), 1.8–1.2 (m, 9H), 0.15 (s, 9H). Anal. Calcd for $C_{14}H_{24}Si$: C, 76.28; H, 10.97. Found: C, 76.77; H, 10.86.

***cis*-2-(3-Bromo-3-butenyl)-1-[(trimethylsilyl)ethynyl]-cyclopentane (9).** Enyne **1** (2 g, 11.1 mmol) was subjected to the cyclization procedure in THF. CuCN·2LiCl (11.6 mL, 1 M in THF, 11.6 mmol) was subsequently added. The greenish solution of the corresponding organozinc copper reagent was stirred for 10 min at 0 °C. It was then cooled to −40 °C, as freshly distilled 2,3-dibromopropene (2.6 g, 13 mmol) was added via syringe. The reaction mixture was slowly allowed to warm to room temperature overnight, and it was then quenched with a saturated NH_4Cl 32%/NH_4OH 2/1 solution. After usual workup, the crude material was purified by flash chromatography (eluent, pentane) to give 2.8 g (72%) of the title compound **9** as a colorless oil. ^{1}H NMR (200 MHz): δ 5.56 (d, J = 0.95 Hz), 5.45 (d, J = 1.38 Hz), 2.75 (m, 1H), 2.4 (q, J = 0.96 Hz, 2H), 1.9–1.4 (m, 9H), 0.15 (s, 9H). ^{13}C NMR (50 MHz): δ 135.1, 116.1, 108.1, 86.8, 42.5, 40.5, 35.1, 33.3, 27.0, 23.2, 19.8, 0.3. Anal. Calcd for $C_{14}H_{23}SiBr$: C, 56.18; H, 7.74. Found: C, 56.55; H, 7.49.

1-(Trimethylsilyl)-3-methoxyoct-7-en-1-yne (10). A solution of bis(trimethylsilyl)acetylene (2.55 g, 0.015 mol) in dry THF (40 mL) was cooled to −30 °C as methyllithium (11.7 mL, 1.28 M in ether prepared from CH_3Br, 0.015 mol) was added rapidly. After the solution was stirred for 2 h at 20 °C, 5-hexen-1-al (1.27 g, 13 mmol) was introduced at −30 °C and the reaction mixture was allowed to warm to room temperature. Methyl iodide (1.5 mL, 24 mmol) was then added in 50 mL of DMSO, and the resultant mixture was heated at 50 °C for 1 h, cooled to −30 °C, and carefully poured into a cold saturated NH_4Cl solution. The layers were separated, and the aqueous one was extracted with ether (2 × 50 mL). The combined extracts were dried over $MgSO_4$. The solvents were evaporated, and the residue was purified by chromatography (eluent, pentane/ethyl acetate 98/2) to give 2.55 g (81%) of the title compound **10** as a colorless liquid. ^{1}H NMR (200 MHz): δ 5.7 (ddt, J = 17.1, 10.3, 6.6 Hz, 1H), 4.8 (m, 2H), 3.84 (t, J = 6.4 Hz, 1H), 3.3 (s, 3H), 2 (m, 2H), 1.5 (m, 4H), 0.13 (s, 9H). ^{13}C NMR (22.6 MHz): δ 138.5, 114.9, 104.7, 90.5, 63.0, 56.3, 35.1, 33.5, 24.6, 0.0.

1-Methoxy-2-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (12). Enyne **10** (450 mg, 2.16 mmol) was subjected to both cyclization in THF and hydrolysis procedures as described above in the typical procedure, except for the use of nBuLi in this case. The crude product was purified by flash chromatography (eluent, pentane/ethyl acetate 98/2) to give 365 mg (80%) of the title compound **12** as a colorless liquid. ^{1}H NMR (200 MHz): δ 3.39 (s, 3H), 2.1–1.8 (m, 7H), 1.08 (d, J = 6.6 Hz, 3H), 0.2 (s, 9H). ^{13}C NMR (22.6 MHz): δ 105.2, 92.2, 85.1, 52.5, 43.8, 37.7, 31.7, 21.3, 17.2, 0.1. Anal. Calcd for $C_{12}H_{22}SiO$: C, 68.51; H, 10.54. Found: C, 68.34; H, 10.48.

***cis*-2-(Iodomethyl)-1-methoxy-1-[(trimethylsilyl)ethynyl]cyclopentane (13).** Enyne **10** (454 mg, 2.16 mmol) was subjected to the cyclization procedure in THF, as described above in the typical procedure, except for the use of nBuLi in this case. Then the reaction mixture was cooled with an ice–water bath as an excess of solid iodine (2–3 equiv) was added. After the mixture was stirred for 10 min at room temperature, 1 M hydrochloric acid (10 mL) and ether (10 mL) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$ and dilute $Na_2S_2O_3$. They were then stirred

for at least 3 h with a few $Na_2S·9H_2O$ crystals. These were then removed by filtration, and the organic solution was washed with brine, dried over $MgSO_4$, and concentrated. The crude material was purified by flash chromatography (eluent, pentane/ethyl acetate 98/2) to give 550 mg (76%) of the title compound **13** as a pale yellow oil. ^{1}H NMR (200 MHz): δ 3.43 (A part of ABX, J_{AB} = 9 Hz, J_{AX} = 3.4 Hz, 1H), 2.98 (B part of ABX, J_{AB} = 9 Hz, J_{BX} = 11 Hz, 1H), 3.27 (s, 3H), 2.4–1.3 (m, 7H), 0.12 (s, 9H). ^{13}C NMR (50.3 MHz): δ 103.2, 93.9, 83.6, 52.7, 52.2, 39.0, 31.3, 20.6, 8.5, 0.2. Anal. Calcd for $C_{12}H_{21}ISiO$: C, 42.86; H, 6.29. Found: C, 42.94; H, 6.44.

1-(Trimethylsilyl)oct-7-en-1-yn-3-ol. (Trimethylsilyl)propynal (11 g, 87.3 mmol) was dissolved in dry Et_2O (100 mL) at −40 °C, as pent-4-en-1-ylmagnesium bromide was added slowly. The cooling bath was removed, and the reaction mixture was heated at 20 °C. After the mixture was stirred for 10 min at room temperature, 1 M hydrochloric acid (10 mL) and ether (10 mL) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude material was purified by distillation under reduced pressure, bp = 75 °C (0.15 Torr), to give 16.25 g (95%) of the title compound as a colorless oil. IR (film): 3700, 3060, 2950, 2895, 2850, 2160, 1680, 1455, 1245, 1120, 1065, 1030, 995. ^{1}H NMR (400 MHz): δ 5.64 (ddt, J = 16.96, 10.31, 6.64 Hz, 1H), 5 (m, 2H), 4.19 (ddd, J = 6.9, 5.04, 6.41 Hz, 1H), 1.93 (m, 2H), 1.64 (m, 1H), 1.53 (m, 2H), 1.39 (m, 2H), 0.17 (s, 9H). ^{13}C NMR (50.3 MHz): δ 138.5, 114.9, 107.1, 89.2, 62.6, 37.1, 33.4, 24.5, 0.1.

1-(Trimethylsilyl)-3-[(thexyldimethylsilyl)oxy]oct-7-en-1-yne (14). To 1.3 g (6.6 mmol) of the preceding alcohol in 10 mL of dry DMF was added 480 mg (7.05 mmol) of imidazole followed by the introduction of thexyldimethylchlorosilane (1.18 g, 6.6 mmol) and a catalytic amount of DMAP. The reaction mixture was stirred for 4 h at room temperature, and 1 M hydrochloric acid (10 mL) and ether (30 mL) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude material was purified by flash chromatography (eluent, pentane/ethyl acetate 98/2) to give 2 g (92%) of the title compound **14** as a pale yellow oil. ^{1}H NMR (400 MHz): δ 5.78 (ddt, J = 17.04, 10.17, 6.87 Hz, 1H), 5 (m, 2H), 4.3 (t, J = 6.33 Hz, 1H), 2.05 (dt, J = 7.15, 6.87 Hz, 2H) 1.7–1.4 (m, 5H), 0.87 (d, J = 6.87 Hz, 3H), 0.86 (d, J = 6.87 Hz, 3H), 0.83 (s, 3H), 0.82 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.11 (s, 9H). ^{13}C NMR (100 MHz): δ 138.9, 114.6, 108.1, 88.5, 63.2, 38.0, 34.3, 33.5, 25.2, 24.6, 20.4, 20.3, 18.8, 18.7, 0.0, −2.2, −2.9.

1-(Trimethylsilyl)-3-[[(methoxyethoxy)methyl]oxy]oct-7-en-1-yne (15). To 1.3 g (6.6 mmol) of the preceding alcohol in 10 mL of dry CH_2Cl_2 were introduced diisopropylethylamine (0.8 mL, 6.6 mmol) and (2-methoxyethoxy)methyl chloride (820 mg, 6.6 mmol), at room temperature. The reaction was stirred overnight, and 1 M hydrochloric acid (10 mL) and ether (30 mL) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude material was purified by flash chromatography (eluent, pentane/ethyl acetate 80/20) to give 1.95 g (98%) of the title compound **14** as a pale yellow oil. ^{1}H NMR (400 MHz): δ 5.78 (m, 5H), 5 (d, 1H, J = 6.87 Hz, 1H), 4.9 (m, 2H), 4.68 (d, 1H, J = 6.87 Hz, 1H), 4.33 (t, J = 6.5 Hz, 1H), 3.74 (m, 1H), 3.62 (m, 1H), 3.53 (m, 2H), 3.37 (s, 3H), 2.06 (m, 2H), 1,68 (m, 2H), 1.54 (m, 2H), 0.13 (s, 9H). ^{13}C NMR (100 MHz): δ 138.5, 114.8, 104.3, 93.1, 90.4, 71.8, 67.3, 66.0, 59.1, 35.0, 33.4, 24.6, 0.0.

1-[(Thexyldimethylsilyl)oxy]-2-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (16). Enyne **14** (400 mg, 1.2 mmol) was subjected to the cyclization in THF and hydrolysis procedures as described above in the typical procedure, except for the use of n-BuLi in this case. The crude product was purified by flash chromatography (eluent, pentane/ethyl acetate 98/02) to give 318 mg (80%) of the title compound **16** as a colorless liquid. ^{1}H NMR (400 MHz): δ 2–1.2 (m, 7H), 0.95 (d, 3H, J = 6.60 Hz), 0.86 (d, 3H, J = 6.88 Hz), 0.95 (d, 3H, J = 6.87 Hz), 0.85 (d, 3H, J = 6.88 Hz), 0.78 (s, 6H), 0.19 (s, 3H), 0.18 (s, 3H), 0.14 (s, 9H). ^{13}C NMR (100 MHz): δ 108.3, 90.6, 79.7, 46.8, 41.6, 34.4, 30.2, 24.9, 20.6, 20.3, 18.8, 18.7, 16.3, 0.0, −0.9, −1.0.

1-[[(Methoxyethoxy)methyl]oxy]-2-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (17). Enyne **15** (400 mg, 1.4 mmol) was subjected to the cyclization in THF and hydrolysis procedures as described above in the typical procedure, except for the use of n-BuLi in this case. The crude product was purified by flash chromatography (eluent, pentane/ethyl acetate 90/10) to give 323 mg (81%) of the title compound **17** as a colorless liquid. ^{1}H NMR (400 MHz): δ 4.96 (d, J = 7.15 Hz, 1H), 4.71 (d, J = 6.87 Hz, 1H), 3.62 (m, 1H), 3.5 (m, 1H), 3.39 (m, 2H), 3.21 (s, 3H), 1.9 (m, 2H), 1.8 (m, 2H), 1.7 (m, 2H), 1.5 (m, 2H), 1.1 (m, 1H), 0.86, (d, J = 6.87 Hz, 3H), 0.12 (s, 9H). ^{13}C NMR (100 MHz): δ 104.4, 92.7, 92.4, 84.6, 71.8, 67.4, 59.1, 44.4, 39.2, 30.4, 20.8, 16.4.

1-Ethynyl-2-methylcyclopentan-1-ol (18). **16** (853 mg, 2.5 mmol) in dry THF (15 mL) was treated at −20 °C by 1 equiv of tetrabutylammonium fluoride (2.6 mL, solution 1N in THF, 2.6 mmol), and the reaction mixture was stirred overnight at room temperature. After usual workup, the crude product was purified by flash chromatography (eluent, pentane/ethyl acetate 90/10) to give 308 mg (99%) of the title compound **18** as a colorless liquid. ^{1}H NMR (400 MHz): δ 2.45 (s, 1H), 2.3 (m, 1H), 2 (m, 4H), 1.7 (m, 2H), 1.3 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz): δ 87.0, 79.8, 75.2, 47.0, 42.2, 32.4, 21.9, 15.7.

1-[(Thexyldimethylsilyl)oxy]-1-ethynyl-2-methylcyclopentane (19). **16** (683 mg, 2 mmol) in wet DMF (15 mL) was treated at 0 °C by an excess of potassium fluoride, and the reaction mixture is stirred overnight at room temperature. After usual workup, the crude product was purified by flash chromatography (eluent, pentane/ethyl acetate 90/10) to give 529 mg (98%) of the title compound **19** as a colorless liquid. ^{1}H NMR (400 MHz): δ 2.47 (s, 1H), 2–1.2 (m, 7H), 1 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.87 Hz, 3H), 0.87 (d, J = 6.87 Hz, 3H), 0.8 (s, 6H), 0.21 (s, 3H), 0.20 (s, 3H). ^{13}C NMR (100 MHz): δ 89.9, 80.1, 75.3, 47.8, 42.5, 35.2, 30.9, 26.0, 21.6, 21.5, 21.4, 19.6, 19.5, 16.9, 0.1, 0.2.

8-(Trimethylsilyl)-6-methyl-1-octen-7-yne (20). 1-Butyne (4.5 l, 0.2 mol) was dissolved in dry THF (300 mL) at −10 °C. The solution was cooled between −30 and −10 °C as *n*-butyllithium (310 mL, 1.6 M in hexanes, 0.5 mol) was added slowly. The cooling bath was removed, and the reaction mixture was heated at 20 °C. At this point, a slightly exothermic reaction started and the temperature rose to 30 °C. The resultant yellow-orange suspension of 1,3-dilithio-1-butyne was heated at 30–35 °C for further 2 h. It was then cooled to −40 °C as 1-bromo-4-pentene (30 g, 0.2 mol) was added rapidly. The cooling bath was removed immediately, and above −20 °C, the temperature began to rise more rapidly. After the mixture was stirred for 30 min, dry HMPA (40 mL) was added and the orange suspension had almost completely disappeared and was replaced by a greenish solution, which was further heated for 1 h at 40–50 °C. It was then cooled to −20 °C as trimethylchlorosilane (25.3 mL, 0.2 mol) was added. The resultant mixture was heated again for 1 h at 50 °C, cooled to 0 °C, and poured into 1 M hydrochloric acid. It was extracted twice with ether, and the combined extracts were washed again with 1 M hydrochloric acid, dried over $MgSO_4$, and evaporated. The crude material was distilled under reduced pressure, bp = 91–95 °C (13 Torr), to give 20.9 g (54%) of the title compound **20** as a colorless oil. ^{1}H NMR (400 MHz): δ 5.79 (ddt, J = 17.0, 10.3, 6.8 Hz, 1H), 5.02–4.89 (m, 2H), 2.4 (m, 1H), 2 (m, 2H), 1.5 (m, 4H), 1.15 (d, J = 6.6 Hz, 2H), 0.13 (s, 9H).

(1*S,2*R**)-2-Methyl-1-methyl-1-[(trimethylsilyl)ethynyl]-cyclopentane (23).** Enyne **20** (200 mg, 1.03 mmol) was subjected to the cyclization in THF and hydrolysis procedures as described above in the typical procedure. The crude product was purified by flash chromatography (eluent, pentane) to give 131 mg (65%) of the title compound **23** as a colorless liquid. ^{1}H NMR (400 MHz): δ 1.95 (s, 1H), 1.73 (m, 2H), 1.73 (m, 2H), 1.58–1.38 (m, 4H), 1.19 (s, 3H), 1.00 (d, J = 6.05 Hz, 3H), 0.13 (s, 9H). ^{13}C NMR (100 MHz): δ 112.5, 85.6, 45.3, 43.2, 41.6, 32.4, 25.7, 21.4, 15.3, 0.35.

(1R*,2R*)-2-(Iodomethyl)-1-neopentyl-1-[(trimethylsilyl)ethynyl]cyclopentane (24). The metallated enyne **21Li** was synthesized according to the literature, and zinc bromide (1 M in ether, 1−1.3 equiv) was added dropwise at −30 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for a further 10 min before iodine (1 g, 3.94 mmol) was added. After usual workup, the crude material was purified by chromatography (eluent, pentane) to give 248 mg (63%) of the title compound as a slightly pale yellow oil. ^{1}H NMR (400 MHz): δ 3.40 (A part of ABX, J_{AB} = 9.35 Hz, J_{AX} = 3.30 Hz, 1H), 3.16 (B part of ABX, J_{AB} = 9.35 Hz, J_{BX} = 11.5 Hz, 1H), 2.28 (m, 1H), 2.04 (m, 1H), 1.79−1.75 (m, 3H), 1.75−1.40 (m, 4H), 1.03 (s, 9H), 0.13 (s, 9H). ^{13}C NMR (100 MHz): δ 109.6, 89.7, 55.3, 52.6, 46.9, 42.5, 32.2, 31.7, 31.4, 31.2, 21.2, 9.00, 0.20. Anal. Calcd for $C_{16}H_{29}SiI$: C, 51.05; H, 7.77. Found: C, 51.12; H, 7.94.

(Z)-(1S*,2R*)-2-(Iodomethyl)-1-neopentyl-1-[2-(trimethylsilyl)ethenyl]cyclopentane (25). To a solution of **24** (100 mg, 0.265 mmol) in dry ether (0.5 mL) was added DIBAL-H (0.5 mL, 1 M in heptane, 0.5 mmol), and the resultant mixture was heated at 40−50 °C for 4 h. It was then cooled to 0 °C and poured into 1 M hydrochloric acid overlaid with ether. The aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$ and evaporated to give a crude material, which was purified by chromatography (eluent, pentane) to give 77.1 mg (77%) of the title compound **25** as a colorless oil. ^{1}H NMR (400 MHz): δ 6.32 (d, J = 15.9 Hz, 1H), 5.54 (d, J = 15.9 Hz, 1H), 3.42 (A part of ABX, J_{AB} = 9.35 Hz, J_{AX} = 3.3 Hz, 1H), 2.82 (B part of ABX, J_{AB} = 9.35 Hz, J_{BX} = 11.7 Hz, 1H), 2.04 (m, 2H), 1.90−0.91 (m, 16H), 0.93 (s, 9H), 0.16 (s, 9H). ^{13}C NMR (100 MHz): δ 153.8, 127.9, 55.7, 55.1, 53.8, 33.5, 32.7, 31.8, 31.1, 21.8, 11.2, 1.7.

3-Methyl-8-(trimethylsilyl)-1-octen-7-yne (27). A solution of bis(trimethylsilyl)acetylene (4.43 g, 26 mmol) in dry THF (50 mL) was cooled to −30 °C as methyllithium (15.5 mL, 1.55 M in ether, 24 mmol) was added. The reaction mixture was stirred for 2 h at room temperature. 6-Iodo-3-methyl-1-hexene (**26**) (4.5 g, 20.1 mmol) was added, followed by dry HMPA (20 mL), which caused the temperature to raise over 40 °C. The reaction mixture was then stirred at −50 °C for 40 min, cooled to 0 °C, and poured into 1 M hydrochloric acid (100 mL). The layers were separated, and the aqueous one was extracted with ether (3 × 50 mL). The combined extracts were washed with saturated $NaHCO_3$ and dilute $Na_2S_2O_3$ and dried over $MgSO_4$. The solvents were evaporated, and the crude material was distilled under reduced pressure, bp = 95−97 °C (13 Torr), to give 2.88 g (74%) of the title compound **17** as a colorless oil. ^{1}H NMR (400 MHz): δ 5.68 (ddd, J = 17.05, 9.9, 7.15 Hz, 1H), 4.96 (d, J = 17.05 Hz, 1H), 4.92 (d, J = 9.9 Hz, 1H), 2.20 (t, J = 7.14 Hz, 2H), 2.13 (m, 1H), 1.53−1.47 (m, 2H), 1.40−1.35 (m, 2H), 0.99 (d, J = 6.6 Hz, 3H), 0.15 (s, 9H). ^{13}C NMR (50 MHz): δ 144.6, 112.8, 107.7, 84.6, 37.5, 35.9, 26.5, 20.4, 20.1, 0.37.

(1S*,2R*,3S*)-2-(Iodomethyl)-3-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (29). Enyne **27** (1 g, 5.15 mmol) was subjected to both cyclization in THF and iodinolysis procedures as described above for the preparation of **5**. The crude material was purified by flash chromatography (eluent, pentane) to give 1.45 g (88%) of the title compound **29** as a colorless oil. ^{1}H NMR (500 MHz): δ 3.35−3.31 (m, 2H), 3.05 (m, 1H), 2.10 (m, 1H), 1.90 (m, 1H), 1.82 (m, 1H), 1.8 (m, 1H), 1.75 (m, 1H), 1.3 (m, 1H), 1.01 (d, J = 6.6 Hz, 3H), 0.15 (s, 9H); ^{13}C NMR (100 MHz): δ 107.6, 87.7, 53.9, 38.6, 36.9, 33.8, 30.8, 19.6, 8.0, 0.37. Anal. Calcd for $C_{12}H_{21}SiI$: C, 45.00; H, 6.61. Found: C, 45.26; H, 6.78.

(Z)-(1S*,2R*,3S*)-2-(2-Butenyl)-3-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (30). Enyne **27** (300 mg, 1.55 mmol) was subjected to the cyclization procedure in THF. Solutions of (Z)-1-iodo-1-propene (prepared from (Z)-propenyllithium (6.7 mL, 0.72 M in ether, 4.8 mmol) and iodine (1.14 g, 4.5 mmol) at −30 °C) and $Pd(PPh_3)_4$ (121.2 mg, 0.10 mmol) in dry THF (15 mL) were combined at room temperature, and the resultant mixture was immediately heated at 35 °C for 1 h. It was then hydrolyzed and worked up as described for the preparation of **6**. The crude material was purified by flash chromatography (eluent, pentane) to give 243 mg (67%) of the title compound **30** as a colorless liquid. ^{1}H NMR (200 MHz): δ 5.46 (m, 2H), 2.86 (m, 1H), 2.20 (m, 2H), 2.05−1.77 (m, 3H), 1.66 (dd, J = 6.8, 0.73 Hz, 3H), 1.4−1.05 (m, 3H), 0.98 (d, J = 6.64 Hz, 3H), 0.13 (s, 9H). ^{13}C NMR (50 MHz): δ 130.1, 124.3, 109.9, 86.6, 51.5, 37.9, 35.5, 32.8, 31.7, 28.1, 19.8, 13.2, 0.45. Anal. Calcd for $C_{15}H_{26}Si$: C, 76.84; H, 11.18. Found: C, 76.68; H, 11.35.

6-Iodo-1-(trimethylsilyl)-1-hexyne (31). A solution of bis(trimethylsilyl)acetylene (24 g, 0.14 mol) in dry THF (200 mL) was cooled to −30 °C as methyllithium (108 mL, 1.33 M in ether, 0.14 mol) was added rapidly. The reaction mixture was then warmed to room temperature and stirred for a further 2 h. 4-Chloro-1-iodobutane (29.5 g, 0.135 mol) was added all at once, and the resultant mixture was heated at 50 °C for 2 h. Dry HMPA (50 mL) was then added, and the reaction mixture was stirred overnight at room temperature. It was then hydrolyzed with 1 M hydrochloric acid (100 mL), the layers were separated, and the aqueous one was extracted with ether (3 × 50 mL). The combined extracts were washed with 1 M hydrochloric acid, saturated brine and dilute $Na_2S_2O_3$, dried over $MgSO_4$, and evaporated. The crude material was distilled under reduced pressure, bp = 91 °C (12 Torr), to give 21 g (82%) of 6-chloro-1-(trimethylsilyl)-1-hexyne as a colorless liquid. ^{13}C NMR (22.4 MHz): δ 106.6, 85.3, 44.5, 31.75, 26.0, 19.3, 0.35.

To a solution of sodium iodide (33.3 g, 0.22 mol) in acetone (150 mL) was added the preceeding compound (21 g, 0.11 mol), and the resultant mixture was refluxed for 48 h. It was then quenched with dilute $Na_2S_2O_3$ and extracted with ether. The combined extracts were dried over $MgSO_4$ and concentrated. The crude material was distilled under reduced pressure, bp = 70 °C (0.5 Torr), to give 26.3 g (84%) of the title compound **31** as a colorless oil. ^{13}C NMR (22.4 MHz): δ 106.5, 85.4, 32.6, 29.4, 19.1, 6.2, 0.35.

2-Methyl-8-(trimethylsilyl)-1-octen-7-yne (32). A suspension of $CuBr{\cdot}Me_2S$ (9.23 g, 44.9 mmol) in dry ether (50 mL) was cooled to −40 °C as isopropenyllithium (80 mL, 1.08 M in ether, 86.4 mmol) was added dropwise. After the addition, the resultant mixture was allowed to warm to −30 °C, and a greenish solution of the organocuprate reagent was obtained. Dry THF (50 mL) and dry HMPA (20 mL) were succesively added at −30 °C, followed by 6-iodo-1-(trimethylsilyl)-1-hexyne (**31**) (12.3 g, 43.9 mmol) dissolved in dry THF (20 mL). The reaction mixture was warmed to −10 °C, and triethyl phosphite (28 mL) was added. After being stirred for 30 min at 0 °C, the reaction mixture was then carefully quenched with 6 M hydrochloric acid. The layers were separated, and the aqueous one was extracted with ether. The combined extracts were washed with saturated NH_4Cl/32% NH_4OH 2/1, dried over $MgSO_4$, and evaporated, and the crude product was filtered through a short column packed with silica gel and eluted with pentane. The solvent was evaporated and the residue distilled under reduced pressure, bp = 97−99 °C (14 Torr), to give 6.5 g (76%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz): δ 4.69 (d, J = 10.45 Hz, 2H), 2.24 (t, J = 6.6 Hz, 2H), 2.03 (t, J = 6.6 Hz, 2H), 1.71 (s, 3H), 1.52 (m, 4H), 0.14 (s, 9H). ^{13}C NMR (100 MHz): δ 145.5, 109.8, 107.3, 84.3, 37.0, 29.9, 26.4, 22.1, 19.5, 0.35.

(Z)-9-(Trimethylsilyl)-2-nonen-8-yne (37). A suspension of $CuBr{\cdot}Me_2S$ (4.70 g, 22.9 mmol) in dry ether (20 mL) was cooled to −40 °C as (Z)-propenyllithium (61 mL, 0.72 M in ether, 43.9 mmol) was added dropwise. After the addition, the resultant mixture was allowed to warm to −33 °C, and a greenish solution of the organocuprate reagent was obtained. Dry THF (25 mL) and dry HMPA (10 mL) were successively added at −30 °C, followed by 6-iodo-1-(trimethylsilyl)-1-hexyne (**31**) (6.16 g, 22 mmol) dissolved in dry THF (15 mL). The reaction mixture was warmed to −10 °C, and triethyl phosphite (14 mL) was added. After being stirred for 30 min at 0 °C, the reaction mixture was then carefully quenched with 6 M hydrochloric acid. The layers were separated, and the aqueous one was extracted with ether. The combined extracts were washed with a saturated NH_4Cl/32% NH_4OH, dried over $MgSO_4$, and evaporated, and the crude product was filtered through a short column packed with silica gel and eluted with

pentane. The solvent was evaporated and the residue distilled under reduced pressure, bp = 97–100 °C (15 Torr), to give 3.0 g (70%) of the title compound **31** as a colorless oil. IR (film): 3005, 2940, 2920, 2850, 2165, 1655, 1245, 1030, 830, 755, 695 cm^{-1}. ^1H NMR (400 MHz): δ 5.47–5.39 (m, 2H), 2.22 (t, J = 7.15 Hz, 2H), 2.06 (m, 2H), 1.60 (d, J = 6.05 Hz, 3H), 1.57–1.36 (m, 4H), 0.14 (s, 9H). ^{13}C NMR (100 MHz): δ 130.5, 124.2, 107.7, 84.5, 28.8, 28.4, 26.5, 19.9, 12.9, 0.35.

(1*R,2*R**)-2-(Iodomethyl)-2-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane (34).** Enyne **32** (1 g, 5.15 mmol) was subjected to the cyclization procedure in THF (10 mL). After being stirred for 2 h at room temperature, the reaction mixture was iodinolyzed and worked up as usual. The crude material was purified by chromatography (eluent, cyclohexane) to give 1.28 g (78%) of the title compound **34** as a slightly pale brown oil. ^1H NMR (400 MHz): δ 3.45 (A part of AB, J_{AB} = 9.89 Hz, 1H), 3.33 (B part of AB, J_{AB} = 9.9 Hz, 1H), 2.63 (t, J = 7.69 Hz, 1H), 2.05 (m, 1H), 1.88–1.60 (m, 4H), 1.4 (m, 1H), 1.15 (s, 3H), 0.15 (s, 9H). ^{13}C NMR (50 MHz): δ 107.4, 87.9, 45.8, 41.3, 38.1, 31.9, 26.8, 22.4, 20.2, 0.20. Anal. Calcd for $C_{12}H_{21}SiI$: C, 45.00; H, 6.61. Found: C, 45.34; H, 6.74.

(1S*,2S*)-2-Methyl-2-(2-propenyl)-1-[(trimethylsilyl)ethynyl]cyclopentane (35). A solution of iodine (3.8 g, 15 mmol) in dry THF (10 mL) was cooled to −30 °C as vinylmagnesium chloride (6.5 mL, 2.3 M in THF, 15 mmol) was added dropwise. After the mixture was stirred for 5 min at room temperature, $Pd(PPh_3)_4$ (446 mg, 0.39 mmol) was added and the resultant mixture was transferred via cannula into a solution of the cyclic organozinc reagent in THF prepared according to the general procedure from enyne **32** (1.5 g, 7.7 mmol). The reaction mixture was heated at 30 °C for 45 min. It was then hydrolyzed and worked up as usual. The crude material was dissolved in pentane (50 mL), and the catalyst was removed by filtration through a pad of Celite. The solvent was evaporated and the crude product purified by flash chromatography (eluent, pentane) to give 1.08 g (61%) of the title compound **35** as a colorless oil. ^1H NMR (400 MHz): δ 5.90–5.80 (m, 1H), 5.04 (m, 2H), 2.38 (dd apparent t, J = 8.25, 7.7 Hz, 1H), 2.23 (dd, J = 13.7, 7.3 Hz, 1H), 2.08–1.99 (m, 2H), 1.71–1.51 (m, 5H), 0.98 (s, 3H), 0.14 (s, 9H).

2,2-Dimethyl-1-[(trimethylsilyl)ethynyl]cyclopentane (36). Enyne **32** (250 mg, 1.29 mmol) was subjected to the cyclization procedure in THF (10 mL). After being stirred for 3 h at room temperature, the reaction mixture was hydrolyzed and worked-up as usual. The crude material was purified by chromatography (eluent, pentane) to give 143 mg (57%) of the title compound **32** as a colorless oil. ^1H NMR (400 MHz): δ 2.30 (t, J = 8.8 Hz, 1H), 2.03–1.97 (m, 1H), 1.73–1.37 (m, 5H), 1.05 (s, 3H), 0.95 (s, 3H), 0.14 (s, 9H). ^{13}C NMR (100 MHz): δ 109.3, 86.0, 43.3, 42.5, 40.2, 31.7, 28.1, 23.3, 22.0, 0.53. Anal. Calcd for $C_{12}H_{22}Si$: C, 74.14; H, 11.41. Found: C, 74.39; H, 11.75.

Note Added in Proof. After submission of this paper, a study of the palladium-catalyzed intramolecular zinc–ene reactions appeared: Oppolzer, W.; Schröder, F. *Tetrahedron Lett.* **1994**, *35*, 7939.

Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of all compounds (55 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.

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