Conformational Control in the Cyclization of an Unsaturated Vinyllithium: Synthesis of (±)-Laurene

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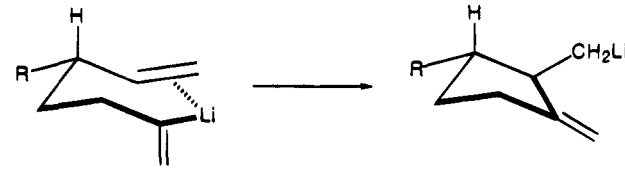
The olefinic vinyllithium **2**, derived from 2-bromo-5-methyl-5-(4-methylphenyl)-1,6-heptadiene (**3**) by low-temperature lithium–bromine exchange, undergoes a diastereoselective 5-exo cyclization at 0 °C in the presence of TMEDA to afford the naturally occurring sesquiterpene (±)-laurene (**1**) in 60% isolated yield along with 17% of the isomeric (±)-epilaurene (**4**). The diastereoselectivity of the cyclization of **2** is discussed in terms of a transition state for the process that approximates a chair cyclohexane which preferentially adopts a conformation having a pseudoaxial *p*-tolyl moiety and a pseudoequatorial methyl group at the geminally substituted carbon. In contrast to the behavior of **2**, radical-mediated cyclization of **3** proceeds entirely in a 6-endo fashion to give 4-methyl-4-(4-methylphenyl)-1-methylenecyclohexane (**6**) in 93% yield.

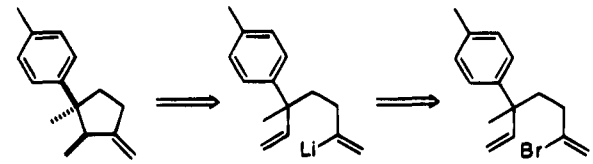
The facile 5-exo ring closure of substituted 5-hexenyllithiums has been used to advantage for the preparation of a variety of five-membered ring-containing carbocycles.[1] This formally anionic cyclization, which has been found to be highly diastereoselective, proceeds via a fairly rigid transition state resembling a chair cyclohexane in which a substituent preferentially occupies a pseudoequatorial position.[2] An equivalent activated complex, shown below, has been proposed by Chamberlin to account for the stereoselective isomerization of the analogous vinyllithium.[3] In light of the excellent regio- and stereocontrol inherent in the cyclization of monosubstituted 5-hexenyllithiums,[1-3] it was of interest to determine whether a more highly substituted system might be prepared in a stereocontrolled fashion using this methodology. To this end, we have investigated the preparation of the naturally occurring sesquiterpene (±)-laurene (**1**) by cyclization of a suitably constituted organolithium. As shown in the sequel, ring closure of a *gem*-disubstituted olefinic vinyllithium proceeds, as expected on the basis of an analysis of the conformational behavior of a chairlike transition state, to give (±)-laurene (**1**) in a single step from the acyclic precursor.



Laurene, which was first isolated as the (+)-enantiomer from *Laurentia glandulifera* and subsequently found in several other Laurentia species,[4] has been prepared by a number of routes.[5] The major synthetic challenge presented by the molecule involves control of the relative stereochemistry at the adjacent quaternary and tertiary centers in **1**, and it is this feature that must be addressed in any cyclization approach to laurene.

Results and Discussion

Simple retrosynthetic analysis of **1**[7] suggests that the carbon framework may be constructed by 5-*exo-trig* cyclization of an olefinic vinyllithium (**2**) which, in turn, can be generated from bromide **3** by low-temperature lithium–halogen exchange.[6]



1 **2** **3**

Clearly, the stereochemical outcome of the cyclization of **2** is crucial to the success of this approach. Given that the 5-exo ring closure of olefinic organolithiums is an operationally irreversible process,[1-3] and on the reason-

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(2) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K.; Ovaska, T. V.; Rossi, K.; Thiel, Y.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 5720.

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(5) For the synthesis of (±)-laurene, see: (a) McMurry, J. E.; von Beroldingen, L. A. *Tetrahedron* **1974**, *30*, 2027. (b) Taber, D. F.; Anthony, J. M. *Tetrahedron Lett.* **1980**, *21*, 2779. (c) Schuda, P. F.; Potlock, S. J.; Ziffer, H. *Tetrahedron* **1987**, *43*, 463. (d) Srikrishna, A.; Sunderbabu, G. *Tetrahedron Lett.* **1989**, *30*, 3561. (e) Srikrishna, A.; Sunderbabu, G. *Tetrahedron* **1991**, *47*, 481. For the synthesis of (+)-laurene, see: Nemoto, H.; Nagamochi, M.; Fukumoto, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1695.

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(7) In the interest of brevity, racemic laurene is represented as a single enantiomer.

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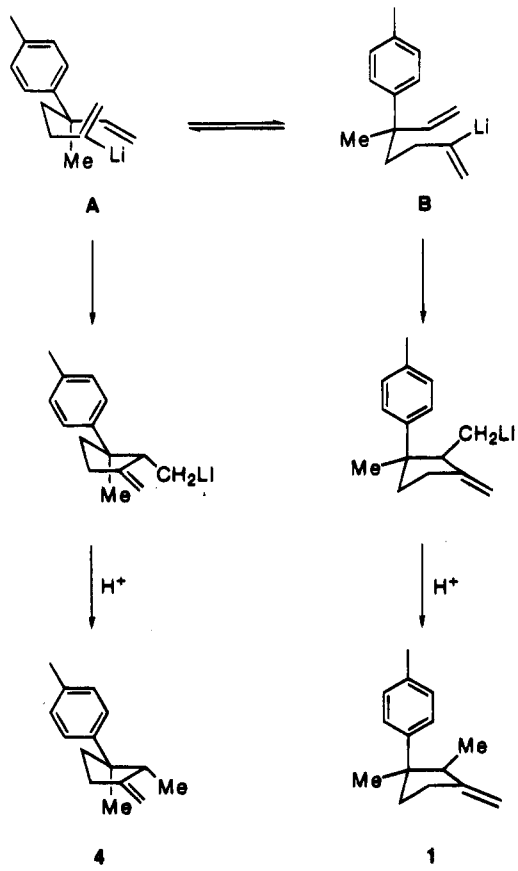
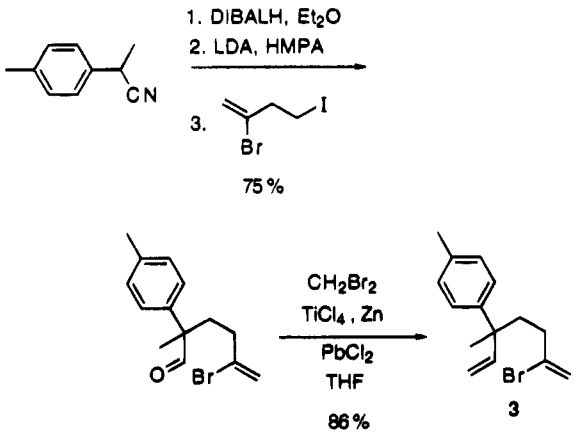
Scheme 1



able assumption that the isomerization proceeds via a chairlike transition state,[2,3] the orientation of the methyl and tolyl substituents in the activated complex determines whether laurene (**1**) or the isomeric epilaurene (**4**) is produced. As illustrated in Scheme 1, two distinct conformationally isomeric chairlike transition states (Scheme 1, **A** and **B**) may be envisioned for the ring closure, and these are interconvertible without loss of the stabilizing interaction of the Li atom at C(1) with the remote π-bond. Thus, successful implementation of this strategy for the preparation of (±)-laurene (**1**) requires that the activation energy for cyclization via transition state **B**, in which the tolyl moiety adopts the pseudoaxial position, is lower than that for the alternative arrangement (**A**) having a pseudoaxial methyl group.

Insofar as the activated complex for ring closure of **2** resembles a chair cyclohexane, the relative energies of transition states **A** and **B** may be evaluated to a first approximation by recourse to the conformational behavior of a cyclohexane model[2] such as 1-methyl-1-phenylcyclohexane. Both molecular mechanics calculations[8,9] and low-temperature NMR studies[9,10] of this geminally disubstituted system have demonstrated that the conformation having the axial phenyl–equatorial methyl arrangement is preferred by approximately 0.3 kcal/mol.[8-10] This simple paradigm suggests that cyclization of **2** should proceed preferentially through a transition state having a pseudoaxial aryl substituent (Scheme 1, **B**) to give laurene. Indeed, a major impetus for the present

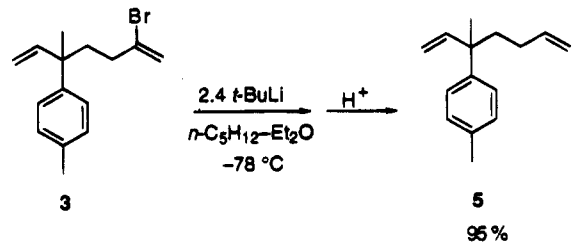
Scheme 2



study was to evaluate the extent to which a substituted cyclohexane could profitably serve as a model for the chairlike activated complex implicated in 5-exo cyclizations of unsaturated organolithiums.

The preparation of vinyl bromide **3** required for the generation of **2** was accomplished as outlined in Scheme 2. Alkylation of the aluminum imide derived from 2-(*p*-tolyl)propanenitrile with 2-bromo-4-iodo-1-butene following the general method of Goering and Tseng[11] proceeded uneventfully in good yield to give an aldehyde which was converted to **3** in 86% yield using the CH_2Br_2–$TiCl_4$–Zn system containing catalytic lead(II).[12]

Treatment of an approximately 0.1 M solution of **3** in *n*-pentane–diethyl ether (3:2 by volume) at −78 °C with 2.2–2.4 molar equiv of *tert*-butyllithium (*t*-BuLi) served to cleanly generate the corresponding vinyllithium (**2**) as demonstrated by the fact that quench of such a reaction mixture delivered 3-methyl-3-(4-methylphenyl)-1,6-heptadiene (**5**) in virtually quantitative yield. It is of some interest to note that there was no evidence of alkyne formation in the lithium–bromine exchange reaction between **3** and *t*-BuLi when conducted using these conditions.[13]



The cycloisomerization of **2** was explored in a series of experiments, summarized in Table 1, in which solutions of the olefinic vinyllithium were allowed to warm and stand at elevated temperature. Not surprisingly,[14] the ring closure of **2** in pentane–ether solution is sluggish even at room temperature (Table 1, entries 2 and 3).

(8) Allinger, N. L.; Tribble, M. T. *Tetrahedron Lett.* **1971**, 3259.
(9) Hodgson, D. J.; Rychlewska, U.; Eliel, E. L.; Monoharan, M.; Knox, D. E.; Olefirowica, E. M. *J. Org. Chem.* **1985**, *50*, 4838.
(10) (a) De Beule, H.; Tavernier, D.; Anteunis, M. *Tetrahedron* **1974**, *30*, 3573. (b) Eliel, E. L.; Monoharan, M. *J. Org. Chem.* **1981**, *46*, 1959.
(11) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1981**, *46*, 5252.
(12) Takai, K.; Kakiuchi, T.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 2668 and references therein.
(13) Formal dehydrohalogenation is a potentially serious complication when vinyl bromides are treated with *t*-BuLi, and for this reason such reactions are often conducted at temperatures below −110 °C to minimize alkyne formation when THF is employed as solvent for the lithium–bromine exchange (Neuman, H.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2785 and references therein). The use of a solvent system containing diethyl ether rather than THF[6] allows for the clean generation of vinyllithiums by lithium–bromine exchange at a more experimentally convenient temperature of −78 °C.

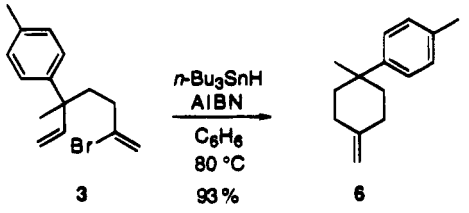
Table 1. Cyclization of Olefinic Vinyllithium 2 (Scheme 3)[a]

entry	additive	temp, °C	time, h	products, % yield[b] laurene (1)	epilaurene (4)	diene 5
1	none	−78	0.5			~100
2		0	1	5	<1	95
3		21	1	24	16	60
4	TMEDA	−30	2	27	4	69
5		−10	2	50	12	38
6		0	1	61	18	21
7		22	1	56	25	19

[a] Olefinic vinyllithium **2** was generated at −78 °C by addition of 2.2−2.4 equiv of *t*-BuLi to a solution of bromide **3** in *n*-pentane−diethyl ether (3:2 by vol). Where indicated, TMEDA was added at −78 °C. The cooling bath was then removed, and the mixture was allowed to stand at the specified temperature for a period of time before the addition of an excess of oxygen-free methanol. [b] Yields were determined by capillary GC and are corrected for detector response.

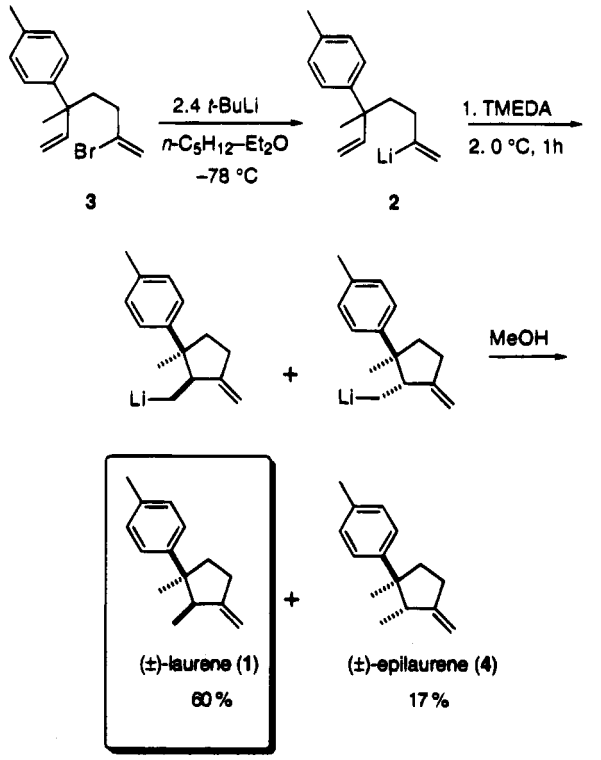
Fortunately, the cyclization of **2** is significantly more facile when *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) is added to the reaction mixture prior to warming. Moreover, inspection of the data presented in Table 1 reveals that isomerization of **2** in the presence of TMEDA is a cleanly 5-exo process that leads, upon quench of the reaction mixtures, to a preponderance of (±)-laurene (**1**). As might be expected, the cyclization of **2** is more diastereoselective at lower temperatures (Table 1, *cf.* entries 4−7): indeed, at −30 °C the ratio of laurene (**1**) to epilaurene (**4**) is approximately 6.7:1. Unfortunately, the higher selectivity at lower temperature is purchased at the expense of a lower yield of cyclic products. Longer reaction times lead to inadvertent quench of the organolithiums by proton abstraction from solvent, and no benefit derives from conducting the isomerizations for periods greater than 1 or 2 h. Nonetheless, preparative scale cyclization of **2** for 1 h at 0 °C in the presence of TMEDA afforded pure (±)-laurene (**1**) in 60% isolated yield along with 17% of the isomeric (±)-epilaurene (**4**) (Scheme 3).

For comparison purposes, the radical-mediated cyclization of **3** was investigated in benzene solution at 80 °C. As expected,[15] the vinyl radical generated from **3** underwent smooth 6-endo closure to give, as shown below, a 93% isolated yield of the methylenecyclohexane (**6**) as the only carbocyclic product. The disparate behavior of the vinyllithium (**2**) and the analogous radical is a rather dramatic example of the often complementary chemistry displayed by these two modes of ring closure.[2,15]



The diastereoselectivity exhibited by the ring closure of **2**, while modest in comparison to the degree of stereocontrol observed in the cyclization of simple, monosubstituted 5-hexenyllithiums,[2] is significant given the steric encumbrance inherent in both the laurene and epilaurene frameworks. A Monte Carlo conformational search using the MM2* parameter set[16] disclosed that the global minimum structure for laurene (**1**) is only 0.68 kcal/mol more stable than that of epilaurene (**4**). Indeed, both **1** and **4** are prone to rearrangement to the more stable 1,2,3-trimethyl-3-(4-methylphenyl)cyclopentene (*i.e.*, isolaurene) in the presence of trace amounts of acid.[5]

Scheme 3



The synthesis of (±)-laurene (**1**) outlined in Scheme 3, coupled with the ease of construction (Scheme 2) of the vinyl bromide precursor **3**, constitutes the most direct preparation to date of the racemic natural product.[5] In a more general sense, the success of this cyclization approach to **1** suggests that cycloisomerization of unsaturated organolithiums may provide access to other sterically encumbered systems. Moreover, the fact that the diastereoselectivity of the cyclization of **2** may be anticipated, at least qualitatively, by analysis of the conformational behavior of chairlike transition states using a cyclohexane model offers the possibility of designing selective approaches to complex systems using anionic cyclization methodology.

Experimental Section

General. General spectroscopic and chromatographic procedures, methods used for the purification of reagents and solvents, and precautions regarding the manipulation of organolithiums have been previously described.[2]

(14) The sluggish cyclization of **2** in the absence of TMEDA is consistent with similar observations made in the course of the preparation the sterically crowded sesquiterpene (±)-cuparene via cyclization of an olefinic alkyllithium: Bailey, W. F.; Khanolkar, A. D. *Tetrahedron* **1991**, *47*, 7727.

(15) (a) Beckwith A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, Essay 4. (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (c) Surzur, J. M. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum: New York, 1982; Vol. 2, Chapter 3. (d) Hart, D. J. *Science* **1984**, *223*, 883. (e) Giese, B. *Radicals in Organic Synthesis*; Pergamon: New York, 1986. (f) Curran, D. P. *Synthesis* **1988**, 417, and 489. (g) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.

(16) Molecular mechanics calculations were performed using the MM2* parameters incorporated in the MacroModel program: Richards, N. G. L.; Guida, W. C.; Liskamp, R.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

The preparation of (4-methylphenyl)acetonitrile (bp 123–125 °C (16 mm) [lit.[17] bp 94–96 °C (3 mm)]) from α-chloro-*p*-xylene followed the procedure described for the synthesis of phenylacetonitrile;[18] 4-iodo-1-butyne (bp 65–67 °C (58 mm) [lit.[19] bp 61 °C (80 mm)]) was prepared from the commercially available alcohol via the mesylate.

2-(4-Methylphenyl)propanenitrile. A solution of 4.00 g (30.5 mmol) of (4-methylphenyl)acetonitrile in 50 mL of dry *N,N*-dimethylformamide was cooled to 0 °C under a nitrogen atmosphere, and 0.80 g (33.3 mmol) of oil-free sodium hydride was added to the solution. The mixture was stirred at 0 °C for 2.5 h, and 4.70 g (33.1 mmol) of methyl iodide was then added dropwise by syringe. The resulting mixture was stirred at room temperature for 18 h and then poured into 150 mL of water, and the mixture was extracted with diethyl ether. The combined ethereal extracts were dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (10% diethyl ether–hexanes; $R_f = 0.37$) to afford 2.88 g (65%) of the known nitrile: ^{1}H NMR δ 1.62 (d, J = 7.26 Hz, 3 H), 2.36 (s, 3 H), 3.87 (q, J = 7.26 Hz, 1 H), 7.18–7.27 (m, 4 H); ^{13}C NMR δ 20.88, 21.33, 30.71, 121.64, 126.45, 129.64, 134.03, 137.68; IR (neat) 2984, 2240, 1513, 1452, 816 cm^{-1}.

2-Bromo-4-iodo-1-butene. Following the general procedure of Hara and co-workers,[21] 35 mL of 1.0 M 9-bromo-9-borabicyclo[3.3.1]nonane (35 mmol) in dichloromethane was diluted with 195 mL of dry dichloromethane under an atmosphere of nitrogen, the solution was cooled to 0 °C, and 5.28 g (29.3 mmol) of 4-iodo-1-butyne was added dropwise. The resulting solution was stirred at 0 °C for 3 h prior to the addition of 19.3 mL of acetic acid. The solution was stirred for an additional 1 h at 0 °C prior to the addition of 233 mL of 3.0 M aqueous sodium hydroxide followed by 38.9 mL of 30% hydrogen peroxide. The resulting two-phase mixture was stirred at room temperature for 30 min, the organic phase was then separated, the aqueous phase was extracted with hexane, and the combined organic extracts were washed successively with 80 mL of water, 60 mL of aqueous saturated sodium bicarbonate, and 80 mL of water. After drying ($MgSO_4$), solvent was removed at reduced pressure and the residue was purified by flash chromatography on silica gel (hexanes; R_f = 0.82) to afford 6.00 g (79%) of the title compound: ^{1}H NMR δ 2.91 (t, J = 6.97 Hz, 2 H), 3.31 (t, J = 6.97 Hz, 2 H), 5.54 and 5.66 (AB pattern, J = 1.60 Hz, 2 H); ^{13}C NMR δ 2.08, 44.87, 118.96, 131.70; IR (neat) 2925, 1630, 1418, 1254, 1170 cm^{-1}. Anal. Calcd for C_4H_6BrI: C, 18.41; H, 2.32. Found: C, 18.59; H, 2.59.

2-Methyl-2-(4-methylphenyl)-5-bromo-5-hexen-1-al. This procedure represents a modification of the general protocol described by Goering and Tseng.[11] A solution of 4.50 g (31.0 mmol) of 2-(4-methylphenyl)propanenitrile in 8.0 mL of dry diethyl ether was cooled to −10 °C, and 31.0 mL of a 1.00 M solution of diisobutylaluminum hydride (31.0 mmol) in hexane was added dropwise. The resulting solution was stirred at −10 °C for 30 min prior to the dropwise addition of 1 molar equiv of LDA (prepared by addition of 21.8 mL of a 1.50 M solution of *n*-BuLi in hexane (32.7 mmol) to 3.13 g (31.0 mmol) of *N,N*-diisopropylamine in 42.0 mL of dry diethyl ether at −78 °C) followed by addition of 6.98 g (38.6 mmol) of hexamethylphosphoric triamide (HMPA). The resulting yellow solution was stirred at room temperature for 1 h and then heated at gentle reflux for an additional 1 h. The mixture was then recooled to −10 °C, and 8.90 g (34.2 mmol) of 2-bromo-4-iodo-1-butene was added dropwise. The resulting solution was stirred at room temperature for 15 h and then heated at reflux for 1 h. The reaction mixture was allowed to cool to room temperature, and 60 mL of 20% aqueous sulfuric acid was added cautiously. The mixture was extracted with three 150-mL portions of diethyl ether, the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was chromatographed on silica gel (10% diethyl ether–hexanes; R_f = 0.58) to afford 6.60 g (75%) of the title aldehyde which was immediately converted into **3**: ^{1}H NMR δ 1.47 (s, 3 H), 2.05–2.08 (m, 2 H), 2.16–2.27 (m, 2 H), 2.35 (s, 3 H), 5.37 and 5.55 (AB pattern, J = 1.89 Hz, 2 H), 7.12–7.22 (m, 4 H), 9.46 (s,1 H); ^{13}C NMR δ 18.64, 20.88, 34.52, 36.31, 52.97, 116.57, 126.94, 129.69, 133.94, 135.80, 137.19, 201.48; IR (neat) 34334, 2924, 1725, 1630, 1512, 1453, 1117, 888, 816 cm^{-1}; HRMS calcd for $C_{13}H_{16}Br$ (M^+ − CHO) 251.0435, found 251.0433.

2-Bromo-5-methyl-5-(4-methylphenyl)-1,6-heptadiene (3). Following the general procedure of Takai and coworkers,[12] 23.5 mL of a 1.00 M solution of titanium tetrachloride (23.5 mmol) in methylene chloride was added dropwise at room temperature under an atmosphere of dry nitrogen to a stirred mixture of 6.31 g (97.1 mmol) of zinc dust, 0.27 g (0.97 mmol) of lead(II) chloride, and 5.56 g (32.0 mmol) of methylene bromide in 90 mL of freshly distilled THF. The resulting mixture was stirred at room temperature for 30 min and then cooled to 0 °C, and a solution of 6.00 g (21.4 mmol) of 2-methyl-2-(4-methylphenyl)-5-hexen-1-al in 15 mL of dry THF was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 4 h then at room temperature for 12 h. The mixture was diluted with 150 mL of diethyl ether, and 100 mL of 5% aqueous hydrogen chloride was cautiously added. The organic phase was separated, washed with two 60-mL portions of brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane; R_f = 0.51) to give 5.10 g (86%) of the title diene: ^{1}H NMR δ 1.41 (s, 3 H), 2.02–2.11 (m, 2 H), 2.27–2.33 (m, 2 H), 2.36 (s, 3 H), 5.07–5.18 (m, 2 H), 5.38 and 5.55 (AB pattern, J = 1.50 Hz, 2 H), 6.04 (d of d, J = 10.78, 17.45 Hz, 1 H), 7.15–7.26 (m, 4 H); ^{13}C NMR δ 20.86, 25.13, 37.09, 39.55, 43.52, 112.16, 115.99, 126.38, 128.96, 135.10, 135.51, 143.67, 146.33. Anal. Calcd for $C_{15}H_{19}Br$: C, 64.52; H, 6.86. Found: C, 64.24; H, 7.17.

3-Methyl-3-(4-methylphenyl)-1,6-heptadiene (5). A flame-dried flask was charged under a blanket of argon with a solution of 0.141 g (0.506 mmol) of 2-bromo-5-methyl-5-(4-methylphenyl)-1,6-heptadiene (**3**) in 3.0 mL of dry *n*-pentane and 2.0 mL of dry diethyl ether. The solution was cooled to −78 °C, and 0.77 mL of a 1.58 M solution of *t*-BuLi (1.22 mmol) in pentane was added dropwise by syringe. The resulting mixture was stirred at −78 °C for 0.5 h and then quenched by addition of 1.0 mL of deoxygenated methanol. The reaction mixture was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexanes; R_f = 0.64) to afford 94.6 mg (95%) of the title diene: ^{1}H NMR δ 1.38 (s, 3 H), 1.74–1.99 (m, 4 H), 2.34 (s, 3 H), 4.90–5.14 (m, 4 H), 5.74–5.86 (m, 1 H), 5.99–6.09 (m, 1 H), 7.12–7.26 (m, 4 H); ^{13}C NMR δ 20.84, 24.98, 28.98, 40.21, 43.84, 111.66, 113.96, 126.45, 128.81, 1354.24, 139.19, 144.28, 146.93; IR (neat) 2599, 1633, 1512, 1456, 1407, 1005, 908, 816 cm^{-1}; HRMS calcd for $C_{15}H_{20}$ 200.1565, found 200.1558.

(±)-Laurene (1). A solution of 0.715 g (2.57 mmol) of 2-bromo-5-methyl-5-(4-methylphenyl)-1,6-heptadiene (**3**) in 10.0 mL of dry diethyl ether and 15.0 mL of dry *n*-pentane was cooled to −78 °C under an atmosphere of dry, oxygen-free argon. The solution was stirred at −78 °C, and 3.91 mL of a 1.58 M solution of *t*-BuLi (6.12 mmol) in pentane was added dropwise via syringe. The mixture was stirred at −78 °C for an additional 5 min after the addition was completed, and 0.716 g (6.16 mmol) of dry *N,N,N',N'*-tetramethylethylenediamine was added via syringe. The reaction mixture was stirred at −78 °C for 5 min, the cooling bath was then removed, and the mixture was allowed to warm and stand at 0 °C for 1 h under an atmosphere of dry argon prior to the addition of 1 mL of deoxygenated methanol. The mixture was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. GC analysis on a 19-m × 0.20-mm 20% methyl phenyl silicone fused-silica capillary column using temperature programming (100 °C for 5 min, 20 °C/min to 250 °C, 250 °C for

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5 min) revealed that three products had formed in a ratio of approximately 3:1:1. The shortest retention time component (*ca.* 20% of the mixture) was identified as 2-methyl-2-(4-methylphenyl)-1,6-heptadiene (**5**) by comparison of GC retention time and mass spectrum with those of an authentic sample. The remaining products were separated by preparative GC on a 10-ft, 5% OV-17 on Chromosorb A column at 135 °C. The major product (309 mg, 60%), which had the longest retention time, was identified as (±)-laurene (**1**) on the basis of the following spectroscopic properties: ^{1}H NMR[22] δ 0.72 (d, J = 7.09 Hz, 3 H), 1.29 (s, 3 H), 1.72–1.86 (m, 2 H), 2.23–2.31 (m, 1 H), 2.33 (s, 3 H), 2.49–2.59 (m, 2 H), 4.88 and 4.89 (apparent two line pattern, 2 H), 7.11 (apparent s, 4 H); ^{13}C NMR δ 17.17, 20.87, 29.19, 29.63, 34.67, 48.95, 50.50, 105.52, 126.87, 128.60, 134.76, 144.45, 157.50; IR (neat) 2959, 1651, 1511, 1450, 1370, 1066, 1023, 871, 804 cm^{-1}. The remaining component (87.4 mg, 17%) was identified as (±)-epilaurene (**4**) on the basis of the following spectroscopic data: ^{1}H NMR[23] δ 0.95 (d, J = 6.72 Hz, 3 H), 1.11 (s, 1 H), 1.77–1.99 (m, 2 H), 2.35 (s, 3 H), 2.39–2.57 (m, 2 H), 2.73–2.74 (m, 1 H), 4.86 and 4.95 (AB pattern, J = 2.38 Hz, 2 H), 7.15–7.33 (m, 4 H); ^{13}C NMR δ 11.75, 19.05, 20.84, 29.63, 39.93, 47.77, 48.53, 105.01, 125.88, 128.84, 135.05, 145.42, 156.55; IR (neat) 2947, 1651, 1511, 1450, 1370, 1017, 907, 877, 815 cm^{-1}.

(22) These ^{1}H NMR shifts are virtually identical to the incomplete proton assignments given by Irie et al. for laurene:[4a,b] *viz.* δ 0.68 (d, J = 7 Hz, 3 H), 1.29 (s, 3 H), 2.31 (s, 3 H), 4.81 (q, J = 1 Hz, 2 H), 6.99 (m, 4 H) [chemical shifts of the remaining five protons in laurene were not reported by Irie et al.].

(23) These ^{1}H NMR shifts are virtually identical to the incomplete proton assignments given by Irie et al. for epilaurene:[4b] *viz.* δ 0.92 (d, J = 7 Hz, 3 H), 1.08 (s, 3 H), 2.33 (s, 3 H), 4.86 (m, 2 H), 6.95–7.30 (m, 4 H) [chemical shifts of the remaining five protons in epilaurene were not reported by Irie et al.].

4-Methyl-4-(4-methylphenyl)-1-methylenecyclohexane (6). A solution of 163 mg (0.585 mmol) of 2-bromo-5-methyl-5-(4-methylphenyl)-1,6-heptadiene (**3**) in 26 mL of dry benzene was heated to reflux under an atmosphere of argon, and 6.00 mL of a solution containing 189 mg (0.649 mmol) of tri-*n*-butyltin hydride and 5 mg of AIBN was added slowly via syringe over a period of 1 h. Following complete addition of the hydride, the reaction mixture was heated at gentle reflux for an additional 2.5 h and then cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography on neutral alumina (hexanes; R_f = 0.59) to give 109 mg (93%) of the title compound: ^{1}H NMR δ 1.28 (s, 3 H), 1.70–1.75 (m, 2 H), 2.16–2.31 (m, 6 H), 2.38 (s, 3 H), 4.66 (apparent s, 2 H), 7.18–7.36 (m, 4 H); ^{13}C NMR δ 20.85, 30.29, 31.46, 37.52, 39.03, 106.57, 125.75, 129.08, 134.88, 145.63, 149.40; IR (neat) 2922, 1645, 1511, 1450, 1377, 1096, 883, 810 cm^{-1}; HRMS calcd for $C_{15}H_{20}$ 200.1565, found 200.1562.

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Supporting Information Available: Copies of the ^{1}H and ^{13}C NMR spectra for all new compounds for which combustion analytical data are not available (6 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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