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FOUR NEW C_{15} ACETYLENIC POLYENES OF BIOGENETIC SIGNIFICANCE FROM THE RED ALGA *LAURENCIA OKAMURAI*: STRUCTURES AND SYNTHESIS

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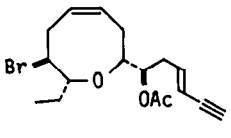
Abstract - From the red alga *Laurencia okamurai* four new C_{15} acetylenic polyenes, laurencenyne 6, neolaurencenyne 7, *trans*-laurencenyne 8, and *trans*-neolaurencenyne 9 have been isolated and their structures were elucidated by chemical and spectral means. Synthesis of these four compounds has been made to confirm their structural and stereochemical assignments. Biogenesis of laurencenyne 6 and *trans*-laurencenyne 8 was discussed.

There have been isolated a large number of halogenated nonterpenoid C_{15} compounds such as laurencin 1,[1] obtusin 2,[2] and *cis*-maneonene A 3[3] from the red algae of the genus *Laurencia*.[4-7] These metabolites were suggested to arise from oxygenation and cyclization of linear C_{15} acetylenic polyenes, which in turn were derived from hexadeca-4,7,10,13-tetraenoic acid.[6,8] This biogenesis was proposed on the basis of the finding that from *Laurencia nipponica trans*- and *cis*-laurediols, 4 and 5 were isolated, which were regarded as the biosynthetic precursors of various nonterpenoid C_{15} metabolites.[8]

We have examined the constituents of the red alga *Laurencia okamurai* collected off the coast of Goza, Mie Prefecture, Japan, in July 1980, and isolated four new acetylenic polyenes, which comprise laurencenyne 6, neolaurencenyne 7, *trans*-laurencenyne 8, and *trans*-neolaurencenyne 9.[9] Evidently, the structures of the acetylenic polyenes, 6 and 8 have close relation with those of laurediols, 4 and 5. This paper describes isolation, structural elucidation, and the synthesis of these four compounds in details.



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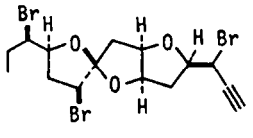

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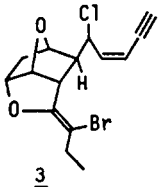

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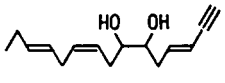

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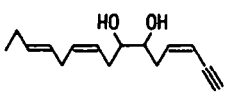

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ISOLATION

The EtOAc soluble fraction of the acetone extract of fresh *L. okamurai* was chromatographed on silica gel with hexane and hexane - benzene (4:1). Subsequently, separation of the fractions eluted with hexane and hexane - benzene (4:1) by TLC on silica gel and reversed-phase HPLC afforded laurencenyne 6 (0.0009%), neolaurencenyne 7 (0.002%), *trans*-laurencenyne 8 (0.0005%), and *trans*-neolaurencenyne 9 (0.0004%), respectively (yields based on the fresh alga). Further, each compound was obtained in pure state by preparative GLC.

Laurencenyne 6: $C_{15}H_{20}$; colorless liquid; UV λ_{max} (MeOH), nm (ε) 224 (13700), 231 (11400, shoulder); IR (film) cm^{-1} 3300 (acetylenic ν_{C-H}), 3010 (olefinic ν_{C-H}), 2140 ($\nu_{C\equiv C}$), 1645 ($\nu_{C=C}$, broad), 725 (δ_{C-H}, *cis* -CH=CH-); ^1H NMR (Table); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 14.3(q), 20.6(t), 25.6(t), 25.7(t), 28.7(t), 80.2(s), 81.8(d), 108.3(d), 126.0(d), 127.0(d), 127.7(d), 128.7(d), 129.6(d), 132.0(d), 143.5(d); MS m/z 200 (M^+).

Neolaurencenyne 7: $C_{15}H_{22}$; colorless liquid; UV λ_{max} (MeOH), nm (ε) 224 (12500), 231 (10600, shoulder); IR (film) cm^{-1} 3300 (acetylenic ν_{C-H}), 3010 (olefinic ν_{C-H}), 2130 ($\nu_{C\equiv C}$), 1640 and 1610 ($\nu_{C=C}$), 730 (δ_{C-H}, *cis* -CH=CH-); ^1H NMR (Table); ^{13}C NMR (25 MHz, $CDCl_3$)[10] δ 14.0(q), 22.5(t), 25.7(t), 27.2(t), 28.7(t), 29.3(t), 31.5(t), 81.7(d), 108.1(d), 125.7(d), 127.3(d), 129.8(d), 130.5(d), 143.5(d); MS m/z 202 (M^+).

trans-Laurencenyne 8: $C_{15}H_{20}$; colorless liquid; UV λ_{max} (MeOH), nm (ε) 223 (13400); IR (film) cm^{-1} 3300 (acetylenic ν_{C-H}), 3010 (olefinic ν_{C-H}), 2170 ($\nu_{C\equiv C}$), 1650 and 1630 ($\nu_{C=C}$), 960 (δ_{C-H}, *trans* -CH=CH-); ^1H NMR (Table); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 14.3(q), 20.6(t), 25.6(t), 25.6(t), 30.6(t), 76.2(d), 82.4(s), 109.1(d), 125.4(d), 127.0(d), 127.5(d), 128.8(d), 130.2(d), 132.1(d), 144.2(d); MS m/z 200 (M^+).

trans-Neolaurencenyne 9: $C_{15}H_{22}$; colorless liquid; UV λ_{max} (MeOH), nm (ε) 223 (15100); IR (film) cm^{-1} 3300 (acetylenic ν_{C-H}), 3010 (olefinic ν_{C-H}), 2150 ($\nu_{C\equiv C}$), 1650 and 1625 ($\nu_{C=C}$), 960 (δ_{C-H}, *trans* -CH=CH-); ^1H NMR (Table); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 14.0(q), 22.6(t), 25.6(t), 27.2(t), 29.3(t), 30.6(t), 31.5(t), 76.2(d), 82.4(s), 108.9(d), 125.0(d), 127.1(d), 130.6(d), 130.7(d), 144.3(d); MS m/z 202 (M^+).

Table ^1H NMR spectral data†

	6	7	8	9
H-1	3.12 (d, 2)	3.11 (d, 2)	2.8 (m)*	2.8 (m)*
H-3	5.4 (m)*	5.4 (m)*	5.4 (m)*	5.4 (m)*
H-4	5.98 (dt, 10, 7)	5.97 (dt, 11, 7)	6.25 (dt, 16, 6)	6.25 (dt, 16, 6)
H-5	3.13 (br dd, 7, 7)	3.13 (br dd, 7, 7)	2.8 (m)*	2.8 (m)*
H-6	5.4 (m)*	5.4 (m)*	5.4 (m)*	5.4 (m)*
H-7	5.4 (m)*	5.4 (m)*	5.4 (m)*	5.4 (m)*
H-8	2.8 (m)*	2.83 (m)	2.8 (m)*	2.8 (m)*
H-9	5.4 (m)*	5.4 (m)*	5.4 (m)*	5.4 (m)*
H-10	5.4 (m)*	5.4 (m)*	5.4 (m)*	5.4 (m)*
H-11	2.8 (m)*	2.07 (m)	2.8 (m)*	2.03 (m)
H-12	5.4 (m)*	1.3 (m)*	5.4 (m)*	1.3 (m)*
H-13	5.4 (m)*	1.3 (m)*	5.4 (m)*	1.3 (m)*
H-14	2.09 (br dq, 7, 7)	1.3 (m)*	2.07 (br dq, 7, 7)	1.3 (m)*
H-15	0.98 (t, 7)	0.90 (br t, 6)	0.98 (t, 7)	0.89 (br t, 6)

† Chemical shifts (δ in ppm) relative to internal TMS. Multiplicities and coupling constants (Hz) are given in parentheses. Spectra were measured in $CDCl_3$ at 100 MHz (6 and 7) and at 90 MHz (8 and 9).

* The exact chemical shift of this signal could not be determined owing to the overlap with other signals.

6

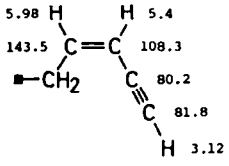
7

8

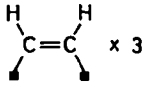
9

STRUCTURES

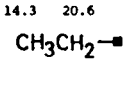
Laurencenyne 6. Catalytic hydrogenation of 6 gave *n*-pentadecane, establishing the carbon skeleton of this compound. Laurencenyne 6 showed spectral properties characteristic of a conjugated *cis*-enyne moiety[3,8,11] (UV 224 and 231 nm; IR 3300, 3010, and 2140 cm^{-1}; ^1H NMR δ 3.12 and 5.98), the presence of which was further corroborated by the ^{13}C NMR spectrum: carbon signals (δ 80.2, 81.8, 108.3, and 143.5) as indicated in the partial structure (I) corresponded well to those of the *cis*-enyne group present in various C_{15} compounds.[3,12,13] Based on the finding that the H-4 signal (δ 5.98) in the partial structure (I) was observed as a doublet of triplets ($J_{3,4}$ = 10 Hz, $J_{4,5}$ = 7 Hz) in the ^1H NMR spectrum of 6, the olefinic carbon (C-4) was deduced to be adjacent to a methylene carbon (C-5) as depicted in (I). The ^1H and ^{13}C NMR spectra of 6 revealed the presence of four disubstituted double bonds, one of which is contained in the partial structure (I). Therefore, there remained three disubstituted double bonds to be characterized. The UV spectral properties and the chemical shifts of the olefinic signals in the ^1H and ^{13}C NMR spectra of 6 indicated that the conjugated enyne group in the partial structure (I) was the only chromophore present in 6. Accordingly, the three disubstituted double bonds to be characterized are unconjugated ones. The *cis* stereochemistry of these three double bonds was inferred on the basis of the fact that no prominent bands around the region of 970 cm^{-1} (δ_{C-H} due to *trans*-disubstituted olefin) were observed in the IR spectrum [partial structure (II)]. Further, an ethyl group (III) was shown to be present in 6 by the ^1H and ^{13}C NMR spectra. Among fifteen carbons in 6, thirteen carbons were characterized (partial structures: I, II, III). Each of the remaining two carbons was readily assigned as a doubly allylic methylene carbon (a di-π-methane carbon), considering their ^1H and ^{13}C NMR spectral properties [partial structure (IV)]. Thus the structure of laurencenyne was deduced to be 6, which was confirmed by the synthesis (*vide post*).



(I)



(II)



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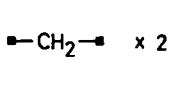


(IV)

Neolaurencenyne 7. Spectral similarity between laurencenyne 6 and neolaurencenyne 7 and the molecular ion peak at m/z 202 in the mass spectrum of 7 suggested the latter 7 to be a dihydro analogue of the former 6. Catalytic hydrogenation of 7 afforded *n*-pentadecane as in the case of 6. The spectral data indicated the presence of the partial structure (I) and two unconjugated *cis*-disubstituted double bonds in 7. Since the chemical shift due to H-5 [partial structure (I)] of 7 was identical with that of the corresponding signal of laurencenyne 6, the methylene carbon (C-5) of the partial structure (I) in 7 was shown to be adjacent to an olefinic carbon (C-6). In the ^1H NMR spectrum of 7 a multiplet ($-CH_2-$) was observed at δ 2.83, which was assigned to doubly allylic methylene protons. These findings clearly defined the location of two *cis*-disubstituted double bonds in the linear pentadecane skeleton, and the structure of neolaurencenyne was deduced to be 7, which was confirmed by the synthesis (*vide post*).

trans-Laurencenyne 8. In view of the similarity of the spectral properties of 8 and laurencenyne 6 together with the fact that the molecular formulas of both compounds are identical, 8 was deduced to be a geometrical isomer of 6. The compound 8 revealed a very strong band at 960 cm^{-1} in the IR spectrum and a characteristic signal at δ 6.25 (1H, dt, J = 16, 6 Hz) in the ^1H NMR spectrum, suggesting that 8 was the *trans* isomer at C-3 of 6. The structure of 8 was unambiguously established as the C-3 *trans* isomer of 6 by comparison of the spectral data of natural 8 with those of authentic 8, the synthesis of the latter being described in this paper (*vide post*).

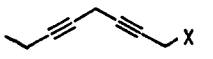
trans-Neolaurencenyne 9. Comparison of the spectral behaviors of neolaurencenyne 7 and 9 suggested the latter 9 to be a *trans* isomer of the former 7. Similarly to the case of *trans*-laurencenyne 8, the compound 9 exhibited a strong band at 960 cm^{-1} in the IR spectrum and a signal at δ 6.25 (1H, dt, J = 16, 6 Hz) in the ^1H NMR spectrum: these findings suggested that 9 was the *trans* isomer at C-3 of 7. This inference was confirmed by the fact that the spectral data of 9 were identical with those of the authentic C-3 *trans* isomer of neolaurencenyne, the synthesis of which is described in the later part of this paper.

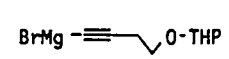
SYNTHESIS

Synthesis of these four acetylenic polyenes, 6, 7, 8, and 9 was performed, which unambiguously confirmed the structural and stereochemical assignments of these natural products described above.

Laurencenyne 6 and *trans*-Laurencenyne 8. The coupling reaction of 1-bromo-2,5-octadiyne 10[14] with the Grignard reagent 12 in the presence of CuCl in THF gave the triyne 11 (67%), which on catalytic hydrogenation in the presence of Lindlar catalyst in benzene afforded the desired all *cis*-triene 13 (68%). Exposure of 13 to methanolic *d*-camphorsulfonic acid provided the triene alcohol 14 (98%), which was converted via sequential reactions with TsCl in pyridine and then NaI in acetone to the triene iodide 15 (78% overall yield) and subsequently with triphenylphosphine in MeCN into the desired phosphonium salt 16 (quantitative). The phosphorane generated from 16 and *n*-BuLi in THF - HMPA was treated with propargylic aldehyde to give, after chromatography on silica gel, a 5.4:1 mixture of 6 and 8 (34%). Separation and purification by preparative GLC afforded 6 and 8, respectively. Stereochemistry of the newly formed double bond (C-3) in the major product 6 was determined to be *cis* from the coupling constant ($J_{3,4}$ = 10 Hz) of H-4 (δ 5.98) in the ^1H NMR spectrum, whereas the minor product 8 was proved to possess the *trans* double bond at C-3 based on the fact that this product 8 exhibited a strong band at 960 cm^{-1} in the IR spectrum and a doublet of triplets due to H-4 at δ 6.25 ($J_{3,4}$ = 16 Hz) in the ^1H NMR spectrum. Synthetic 6 and 8 were completely identical with natural 6 and 8, respectively, in all aspects (IR, ^1H and ^{13}C NMR, and mass spectra, HPLC and GLC retention times, and TLC mobility).

Neolaurencenyne 7 and *trans*-Neolaurencenyne 9. (3Z,6Z)-3,6-Dodecadien-1-ol 17[15] was converted via sequential reactions with TsCl in pyridine and then NaI in acetone to the diene iodide 18 (79% overall yield), which on reaction with triphenylphosphine in MeCN provided the phosphonium salt 19 (91%). The Wittig reaction of propargylic aldehyde with the phosphorane generated from 19 and *n*-BuLi in THF - HMPA afforded, after chromatography on silica gel, a 3:1 mixture of 7 and 9 (43%). Separation and purification by preparative GLC gave 7 and 9, respectively. The *cis* stereochemistry of the newly formed double bond (C-3) in the major product 7 and the *trans* stereochemistry of the corresponding one in the minor product 9 were assigned on the basis of their coupling constants ($J_{3,4}$ = 11 Hz in 7 and $J_{3,4}$ = 16 Hz in 9) in the ^1H NMR spectra and the strong band at 960 cm^{-1} in the IR spectrum of 9. Synthetic 7 and 9 were proved to be identical with natural 7 and 9, respectively, by comparison of the spectral data (IR, ^1H and ^{13}C NMR, and MS) and chromatographic behaviors (HPLC and GLC retention times, and TLC mobility).





10 X = Br
11 X = C≡CCH$_2$CH$_2$O-THP

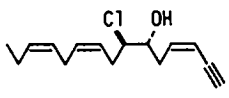
12

13 X = O-THP
14 X = OH
15 X = I
16 X = $PPh_3 \cdot I$

17 X = OH
18 X = I
19 X = $PPh_3 \cdot I$

DISCUSSION

Biogenetic significance of isolation of laurencenyne 6 and *trans*-laurencenyne 8 is evident, because they might be intermediates in the earlier stage of the biosynthetic pathway to a variety of halogenated C_{15} metabolites than laurediols, 4 and 5. It is interesting to note that a chlorinated alcohol 20 was isolated from *L. pinnatifida*,[16] which can be regarded as a chlorohydrin derivative of laurencenyne 6. In connection with the biogenesis of laurepinnacin 21[17] and isolaurepinnacin 22,[17] it is particularly significant that *trans*-laurencenyne 8 was detected in *L. okamurai*: Fukuzawa and Masamune described that these two cyclic ethers, 21 and 22 could not be biogenetically derived from *trans*-laurediol 4 but must be arise from a new, hypothetical precursor 8 from the viewpoint of the stereostructures of 21 and 22.[17] Thus the isolation of *trans*-laurencenyne 8 from *L. okamurai* strongly supports the validity of the biogenesis of the two cyclic ethers, 21 and 22 proposed by Masamune.[17] It is worth noting that both acetylenic polyenes, 6 and 8 isolated from *L. okamurai* in the present study have recently been detected also in *L. nipponica* by Kurosawa and his associates.[18,19]



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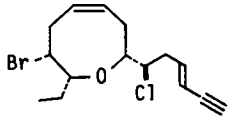

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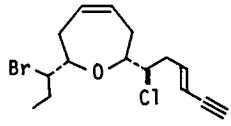

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EXPERIMENTAL

UV spectra were measured on a JASCO UVIDEC-510 spectrophotometer. IR spectra were obtained with a JASCO Model IRS spectrophotometer in $CHCl_3$ solution, unless otherwise noted. ^1H NMR spectra were recorded on JEOL FX-90QE (90 MHz) and Varian HA-100 (100 MHz) instruments in $CDCl_3$: chemical shifts (δ) are reported in ppm downfield from internal TMS and coupling constants in Hz. ^{13}C NMR spectra were measured using JEOL FX-90QE (22.5 MHz) and JNM FX-100 (25 MHz) spectrometers in $CDCl_3$: chemical shifts (δ) are reported in ppm downfield from internal TMS. Mass spectra were recorded on Hitachi RMU-6C and JEOL JMS-DX300 instruments. Fuji-Davison silica gel BW-80 was used for column chromatography. Merck precoated silica gel $60F_{254}$ plates were used for TLC and Merck silica gel PF_{254} for preparative TLC. A Varian 1828-4 gas chromatograph was used for GLC. For HPLC a JASCO TRI ROTAR-II apparatus equipped with a UV detector (JASCO UVIDEC-100-II) and a refractive index detector (Shodex RI SE-11) was used. Organic solutions in the synthetic operations were dried over anhydrous Na_2SO_4 and concentrated by vacuum rotary evaporator.

Isolation of laurencenyne 6, neolaurencenyne 7, *trans*-laurencenyne 8, and *trans*-neolaurencenyne 9. The fresh alga (*L. okamurai*, 2.3 kg) collected in July at Goza, Mie Prefecture, Japan, was extracted with acetone (8 ℓ) at 20 - 25 °C. After filtration the solvent was removed under reduced pressure to give an aqueous residue, which was extracted with EtOAc (2 x 1 ℓ). The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield a greenish oil (13 g). A portion of the oil (6.4 g) was applied to a silica gel (192 g) column and eluted consecutively with 100 ml each of hexane (3.4 ℓ) and hexane-benzene (4:1) (1.5 ℓ). The early fractions (fraction No. 12-19), the middle fractions (fraction No. 20-26), and the later fractions (fraction No. 27-34) eluted with hexane afforded, on evaporation of the solvent, neolaurencenyne 7 (106 mg), *trans*-neolaurencenyne 9 (24 mg), and laurencenyne 6 (33 mg), respectively, in the crude state. From the early fractions (fraction No. 36-39) eluted with hexane-benzene (4:1) there was obtained crude *trans*-laurencenyne 8 (34 mg). Further purification of these four compounds was performed as follows. Crude 6 (33 mg) and crude 7 (106 mg) were separated by reversed-phase HPLC using a ZORBAX ODS column (0.46 x 25 cm) [EtOH-H_2O (9:1), flow rate 1.0 ml/min] to give 6 (10 mg, 0.0009%) (retention time 5.3 min) and 7 (26 mg, 0.002%) (retention time 5.8 min), respectively. Pure 6 and 7 were obtained by preparative GLC using a 10% SILAR 10C on Chromosorb WAW DMCS column (6 mm x 1.5 m) at 135 °C (He as carrier gas; flow rate 65 ml/min); retention time, 6.5 min for 6 and 4.7 min for 7. Separation of crude 8 (34 mg) and crude 9 (24 mg) by preparative TLC was carried out to give 8 (6 mg, 0.0005%) and 9 (5 mg, 0.0004%), respectively. Pure 8 and 9 were obtained by preparative GLC under the same conditions as employed for 6 and 7: retention time, 9.2 min for 8 and 6.4 min for 9. Physical and spectral data of 6, 7, 8, and 9 are listed in the text and Table.
[HRMS. 6, Found: 200.1554 (M^+). $C_{15}H_{20}$ requires: 200.1564. 7, Found: 202.1703 (M^+). $C_{15}H_{22}$ requires: 202.1719. 8, Found: 200.1538 (M^+). $C_{15}H_{20}$ requires: 200.1564. 9, Found: 202.1703 (M^+). $C_{15}H_{22}$ requires: 202.1719.

Catalytic hydrogenation of laurencenyne 6 and neolaurencenyne 7. A solution of 6 (0.7 mg) in EtOH (0.3 ml) in the presence of PtO_2 (1.1 mg) was stirred in the atmosphere of H_2 at room temperature for 1 h and 45 min. After removal of the catalyst by filtration, the filtrate was concentrated to obtain a colorless liquid, which was identified as *n*-pentadecane (0.7 mg) by comparison of the mass spectral data and the GLC behavior using a 10% SILAR 10C column at 98 °C with those of the authentic sample. Following the same procedures as described above, 7 (0.7 mg) was catalytically hydrogenated to afford *n*-pentadecane.

cis-Triene 13. A solution of 3-butyn-1-ol tetrahydropyranyl ether[15] (1.40 g, 9.1 mmol) in THF (2 ml) was added under argon to a stirred 1 M solution of EtMgBr in THF (10 ml, 10.0 mmol) cooled at 0 °C. The mixture was refluxed for 1 h and cooled to room temperature and then Cu(I)Cl (87 mg, 0.9 mmol) was added in one portion. The mixture was kept at reflux for 15 min and cooled to room temperature. To this mixture was added a solution of 10[14] (939 mg, 5.1 mmol) in THF (3 ml) with stirring. The mixture was refluxed for 4 h, cooled to 0 °C, diluted with saturated NH_4Cl solution (10 ml), and concentrated. The aqueous residue was extracted with CH_2Cl_2 (5 x 10 ml). The combined extracts were washed with saturated $NaHCO_3$ solution, dried, and concentrated to give an oily residue, which was chromatographed over silica gel (10:1 hexane-Et_2O), yielding 11 (859 mg, 67%) as a colorless oil: IR 2380, 2290, 1325, 1030 cm^{-1}; ^1H NMR (100 MHz) δ 1.12 (3H, t, J = 7), 1.4-1.9 (6H, m), 2.18 (2H, qt, J = 7, 2), 2.48 (2H, tt, J = 7, 2), 3.14 (4H, m), 3.4-4.0 (6H, m), 5.65 (1H, m); MS m/z 258 (M^+), 257, 153, 85. Chromatographically purified 11 contained a trace amount of unidentified catalyst poisons that could be removed on treatment of 11 with 10% Pd-C prior to catalytic hydrogenation: a mixture of 11 (107 mg, 0.41 mmol) and 10% Pd-C (193 mg) in benzene (6.1 ml) containing 0.01 ml of quinoline was stirred at room temperature for 2 h under nitrogen and then filtered, and the filtrate was concentrated to give an oil. A mixture of the oil and the Lindlar catalyst (12.5 mg) in benzene (5 ml) was stirred in the atmosphere of H_2 at room temperature for 1 h, and then the Lindlar catalyst (41.8 mg) was further added and the stirring was continued for further 6 h. The mixture was filtered and the filtrate was concentrated to afford an oily residue, which was chromatographed on silica gel (15:1 hexane-Et_2O), providing 13 (74 mg, 68%) as a colorless oil: IR 1650, 1140, 1125, 1080, 1030 cm^{-1}; ^1H NMR (100 MHz) δ 0.97 (3H, t, J = 7), 1.4-1.9 (6H, m), 2.08 (2H, dq, J =7, 7), 2.39 (2H, br dt, J = 6, 6), 2.7-2.9 (4H, m), 3.3-4.1 (4H, m), 4.61 (1H, m), 5.1-5.7 (6H, m); MS m/z 264 (M^+), 85 [HRMS. Found: 264.2085 (M^+). $C_{17}H_{28}O_2$ requires: 264.2086].

Triene iodide 15. A solution of 13 (74.3 mg, 0.28 mmol) and *d*-camphorsulfonic acid (6 mg, 0.024 mmol) in MeOH (2 ml) was stirred at room temperature for 45 min. To the mixture was added Et_3N (0.06 ml) and the stirring was continued for 20 min. The mixture was concentrated and the resulting residue was chromatographed on silica gel (4:1 hexane-EtOAc) to afford 14 (49.7 mg, 98%) as a colorless oil: IR 3600, 3400, 3040, 1650, 1045 cm^{-1}; ^1H NMR (100 MHz) δ 0.98 (3H, t, J = 7), 2.08 (2H, br dq, J = 7, 7), 2.37 (2H, dt, J = 6, 6), 2.7-3.0 (4H, m), 3.68 (2H, t, J = 6), 5.2-5.7 (6H, m); MS m/z 180 (M^+), 162, 149. A mixture of 14 (157 mg, 0.87 mmol) and TsCl (199 mg, 1.04 mmol) in pyridine (0.28 ml) was stirred for 3 h at 0 °C, and after additional TsCl (92 mg, 0.48 mmol) was added, stirring was continued for 2 h at 0 °C. Additional pyridine (0.1 ml) was added and the mixture was stirred for 1 h at 0 °C, and then TsCl (99 mg, 0.52 mmol) was further added. After stirring for 30 min, 4-dimethylaminopyridine (*ca.* 2 mg) was added and the mixture was stirred at room temperature for 1 h, diluted with H_2O (4 ml), and extracted with ether (4 x 10 ml). The combined ethereal extracts were washed with H_2O, saturated $CuSO_4$ solution, H_2O, and saturated NaCl solution, and dried. Removal of the solvent afforded the crude tosylate (274 mg, 94%) as a colorless oil, which was employed in the next step without further purification [IR 3030 (shoulder), 1650, 1600, 1365, 1180, 1100, 965 cm^{-1}; ^1H NMR (100 MHz) δ 0.97 (3H, t, J = 7), 2.07 (2H, br dq, J = 7, 7), 2.43 (2H, dt, J = 7, 7), 2.45 (3H, s), 2.6-2.9 (4H, m), 4.04 (2H, t, J = 7), 5.1-5.6 (6H, m), 7.34 (2H, d, J = 8), 7.80 (2H, d, J = 8); MS m/z 334 (M^+), 172]. A mixture of the tosylate (240 mg, 0.72 mmol) and NaI (314 mg, 2.09 mmol) in acetone (4 ml) was stirred at room temperature for 14 h and diluted with H_2O (10 ml). A 1 M solution of $Na_2S_2O_3$ was added to the mixture until coloration due to I_2 disappeared. The mixture was extracted with hexane (4 x 10 ml). The combined organic extracts were washed with H_2O, dried, and concentrated to give a residue, purification of which by preparative TLC on silica gel (hexane) afforded 15 (172 mg, 78% overall from 14) as a colorless oil: IR 3020, 1650, 1240, 1170 cm^{-1}; ^1H NMR (100 MHz) δ 0.99 (3H, t, J = 7), 2.09 (2H, br dq, J = 7, 7), 2.5-2.9 (6H, m), 3.16 (2H, t, J = 6), 5.2-5.8 (6H, m); MS m/z 290 (M^+), 163.

Synthesis of laurencenyne 6 and *trans*-laurencenyne 8. A mixture of 15 (144 mg, 0.50 mmol) and Ph_3P (317 mg, 1.2 mmol) in MeCN (1 ml) was stirred at room temperature for 11 h and at 40 °C for 36 h. Concentration of the mixture afforded an oily residue, which was washed with 1:1 pentane-Et_2O (3 x 5 ml) and Et_2O (3 x 4 ml). The residue was dried *in vacuo* (3 mmHg) to afford 16 (277 mg, quantitative) as a colorless oil: IR 1610, 1590, 1440 (strong), 1110 (strong), 995 cm^{-1}; ^1H NMR (100 MHz) δ 0.97 (3H, t, J = 7), 2.02 (2H, dq, J = 7, 7), 2.4-2.8 (6H, m), 3.78 (2H, m), 5.1-5.8 (6H, m), 7.4-8.0 (15H, m). This material was employed in the next step without further purification. To a stirred mixture of 16 (51 mg, 0.092 mmol) in THF (0.5 ml) - HMPA (0.16 ml) at -78 °C was added a 1.52 M solution of *n*-BuLi in hexane (75 µl, 0.114 mmol) under nitrogen. The mixture was stirred at -78 °C for 20 min and a 10% solution of propargylic aldehyde in Et_2O (60 µl, 0.11 mmol) was added. The mixture was stirred at -78 °C for 1.5 h and then at room temperature for 2 h, diluted with saturated NH_4Cl solution (2 ml) at 0 °C, and extracted with Et_2O (4 x 5 ml). The ethereal extracts were washed with saturated NaCl solution, dried, and concentrated. Purification of the crude product by chromatography on silica gel (hexane) afforded a 5.4:1 mixture of 6 and 8 (6.4 mg, 34% based on 16) as a colorless oil, the ratio of 6 and 8 being determined by GLC analysis with the column described for isolation of 6 and 8 at 140 °C (He as carrier gas; flow rate, 70 ml/min). Separation of the mixture by preparative GLC under the conditions employed for isolation of 6 and 8 (*vide ante*) afforded 6 and 8 as a colorless liquid,

respectively. The IR, ^{1}H NMR, and mass spectra and the GLC behaviors of synthetic 6 and 8 proved identical with those of natural 6 and 8, respectively.

Diene iodide 18. A mixture of 17[15] (70.4 mg, 0.39 mmol) and TsCl (95.9 mg, 0.50 mmol) in pyridine (0.13 ml) was stirred at 0 °C for 6 h. A small amount of ice was added to the mixture. The mixture was stirred at room temperature for 30 min, diluted with H_2O (5 ml), and extracted with Et_2O (4 x 10 ml). The ethereal extracts were washed with H_2O, saturated $CuSO_4$ solution, H_2O, and saturated NaCl solution, and dried. On removal of the solvent a colorless oil of the tosylate (129 mg) was obtained, which was used in the next step without further purification. A mixture of the tosylate (75 mg, 0.22 mmol) and NaI (107 mg, 0.71 mmol) in acetone (0.5 ml) was stirred at room temperature for 15 h and diluted with H_2O (2 ml). A 1 M solution of $Na_2S_2O_3$ was added to the mixture until coloration due to I_2 disappeared. The mixture was extracted with hexane (4 x 5 ml). The combined organic extracts were washed with saturated NaCl solution, dried, and concentrated to afford a residue, purification of which by preparative TLC on silica gel (hexane) gave 18 (52 mg, 79% overall from 17) as a colorless oil: IR 1240, 1170 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.91 (3H, br t, J = 6), 1.2-1.6 (6H, m), 2.06 (2H, m), 2.6-2.9 (4H, m), 3.16 (2H, t, J = 7), 5.2-5.7 (4H, m); MS m/z 292 (M^+), 165 [HRMS. Found: 292.0670 (M^+). $C_{12}H_{21}I$ requires: 292.0686].

Synthesis of neolaurencenyne 7 and *trans*-neolaurencenyne 9. A mixture of 18 (71.2 mg, 0.24 mmol) and Ph_3P (384 mg, 1.46 mmol) in MeCN (1 ml) was stirred at room temperature for 14 h and at 50 °C for 24 h. Concentration of the mixture gave an oily residue, which was washed with 1:1 pentane-Et_2O (3 x 3 ml) and Et_2O (2 x 4 ml). The residue was dried *in vacuo* (2 mmHg) to obtain 19 (121 mg, 91%) as a pale yellow oil: IR 1590, 1440 (strong), 1115 (strong), 995 cm^{-1}; ^{1}H NMR (90 MHz) δ 0.91 (3H, br t, J = 6), 1.1-1.5 (6H, m), 1.91 (2H, m), 2.58 (4H, m), 3.84 (2H, m), 5.1-5.8 (4H, m), 7.5-8.1 (15H, m). This material was employed in the next step without further purification. To a stirred mixture of 19 (44.4 mg, 0.080 mmol) in THF (0.5 ml) - HMPA (0.14 ml) at -78 °C was added a 1.5 M solution of *n*-BuLi in hexane (70 µl, 0.11 mmol) under nitrogen. The mixture was stirred at -78 °C for 20 min and an 8.4% solution of propargylic aldehyde in Et_2O (60 µl, 0.094 mmol) was added. The mixture was stirred at -78 °C for 1 h and at room temperature for 1 h, diluted with H_2O (1.5 ml), and extracted with pentane (5 x 5 ml). The organic extracts were washed with saturated NH_4Cl solution, dried, and concentrated. Purification of the crude product by chromatography on silica gel (pentane) gave a 3:1 mixture of 7 and 9 (7.0 mg, 43% based on 19) as a colorless oil, the ratio of 7 and 9 being determined by HPLC analysis with a Develosil ODS-5 column (0.46 x 25 cm) [EtOH-H_2O (4:1), flow rate 0.6 ml/min]. Separation of the mixture by preparative GLC under the conditions employed for the synthesis of 6 and 8 (*vide ante*) gave 7 and 9 as a colorless liquid, respectively. The IR, ^{1}H NMR, and mass spectra and the GLC behaviors of synthetic 7 and 9 proved identical with those of natural 7 and 9, respectively.

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