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# LAUREPINNACIN AND ISOLAUREPINNACIN, NEW ACETYLENIC CYCLIC ETHERS FROM THE MARINE RED ALGA LAURENCIA PINNATA YAMADA

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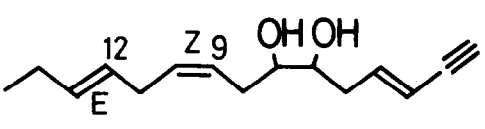
Abstract The Structure elucidation of the title compounds, two new insecticidal components of the marine red alga Laurencia pinnata Yamada, is described.

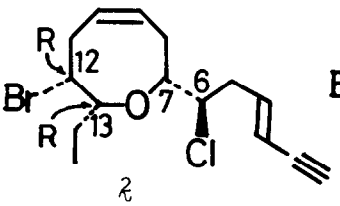
A number of halogenated secondary metabolites with $C_{15}$ vinyl acetylenic or allenic cyclic ether structures have been isolated from the marine red algae genus Laurencia.[1] A survey of the stereostructures of the metabolites reveals that all the reported compounds, with one exceptional example,[2] possess either (12R,13S)- or (12S,13R)-configurations, corresponding to the (12E)-configuration of the potential precursor laurediol[3] (1). We have recently isolated new insecticidal cyclic ethers, designated as laurepinnacin and isolaurepinnacin, from the title alga, in which the relevant carbon atoms are characterized by (12R, 13R)- and (12S,13S)-configurations, respectively. We report herein the structures of the metabolites.

Neutral ether-soluble oil (7.5 g) obtained from methanol extracts of the alga (wet, 4 kg), collected at Motsuta point, Hokkaido, in early July, was fractionated by repeated chromatography over silica gel to yield laurepinnacin (2) (390 mg) and isolaurepinnacin (3) (160 mg).

Laurepinnacin (2), colorless oil, $[\alpha]_D$ -35.3 ($CHCl_3$), had molecular formula $C_{15}H_{20}OClBr$ and displayed the UV and IR spectra[4] indicating the presence of a conjugate enyne unit.[5] Measurement of the $^1H$ NMR spectrum at 400 MHz[6] effected complete separation of all the protons and, combined with spin-decoupling experiments, led to elucidation of the whole planar structure of 2, which was consistent with the $^{13}C$ NMR spectrum.[7] It is noted that the compound (2) differs from intricenyne,[8] a metabolite isolated from L. intricata and assigned the same planar formula. The configurations of C-6, C-7, C-12, and C-13 in 2 were established by chemical correlation with laurencin[5] (4), as described below.




1

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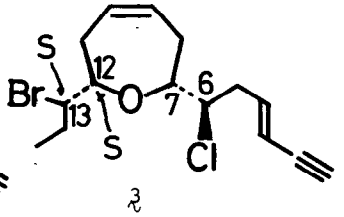


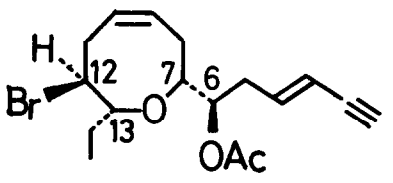

3

Hydrogenation (Pt in EtOH, room temp, 2 h) of 2 afforded octahydrolaurepinnacin (5), $[\alpha]_D$ + 55.0, which underwent stepwise hydrogenolysis over Raney-nickel in ethanol (i, room temp, 1 h, and ii, reflux, 5 h) to give debromo-octahydrolaurepinnacin (6), $[\alpha]_D$ +40.8, and debromodechlorooctahydrolaurepinnacin (7), $[\alpha]_D$ +5.3, in 91 and 71% yields, respectively. On the other hand, deacetyl-octahydrolaurencin[5] (8) was converted by treatment with thionyl chloride (no solvent, reflux, 1.5 h) into the corresponding chloro derivative (9), as a major product (57%). The carbon atom (C-6) bearing the chlorine atom in 9 was assigned the same configuration (R) on the basis of the stereospecificity of the relevant substitution ($S_Ni$) as well as the splitting pattern of the proton at C-6 in 2 (dt, J = 10 and 4 Hz) (cf., the corresponding proton of 4, dt, J = 8 and 5 Hz).[5] Compound 9 was then submitted to successive hydrogenolysis under the aforementioned conditions to give its debromo derivative (10), $[\alpha]_D$ +40.4, and debromo-deacetoxyoctahydrolaruencin (11), $[\alpha]_D$ +4.6, in 88 and 76% yields, respectively. The latter compound was also obtained by tosylation of deacetyldebromooctahydro-laurencin[5] (12) followed by reduction ($LiAlH_4$ in ether, reflux, 1 h) in 85% yield. The former (10) and latter (11) were indistinguishable from 6 and 7, respectively in all respects, ($[\alpha]_D$, MS, IR, $^1H$ NMR, and TLC), while 9 exhibited the IR and $^1H$ NMR spectra different from those of 5. These facts indicate that laurepinnacin is represented by formula 2, which is characterized by the configurations (12R,13R) of both the 12- and 13-carbon atoms.

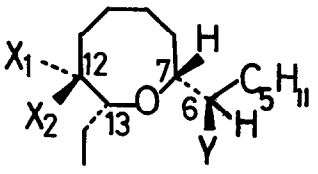
Isolaurepinnacin (3), colorless oil, $[\alpha]_D$ -6.2 ($CHCl_3$), had the same molecular formula $C_{15}H_{20}OClBr$ as 2. The UV, IR, $^1H$ (400 MHz)[6] and $^{13}C$ NMR spectra[7] suggested that 3 would have a structure resembled closely to 2. Hydrogenation (Pt in EtOH, room temp, 2 h) of 3 gave octahydroisolaurepinnacin (13), $[\alpha]_D$ +2.5, which on hydrogenolysis over Raney nickel in ethanol (reflux, 5 h) formed debromodechlorooctahydroisolaurepinnacin (14), $[\alpha]_D$ -2.5, in 64% yield. In contrast with the corresponding laurepinnacin derivative (7) [MS, m/e 197 ($M^+ - C_2H_5$) and 141 ($M^+ - C_6H_{13}$)], the compound (14) showed a strong fragmentation peak at m/e 183 due to a cation ($M^+ - C_3H_7$) with that at m/e 141, indicating that 14 would probably be an oxepane with propyl and hexyl side chains at α- and α'-positions. Compound 13, when treated with zinc in acetic acid and then with acetic anhydride, afforded a mixture of olefins, from which acetates of (12E)- and (12Z)-6-chloropentadec-12-en-7-ols (15), $[\alpha]_D$ +36.5, and (16), $[\alpha]_D$ +42.4, were isolated in 55 and 15% yields as less-polar and more-polar components by chromatography over silver nitrate-impregnated silica gel, respectively. Each of these olefins (15) and (16) were produced by the same treatment of 5 in 66 and 15% yields, respectively: (12E)-isomer $[\alpha]_D$ +34.8; (12Z)-isomer, $[\alpha]_D$ +43.6. The chemical correlation between the two metabolites (2) and (3) indicates that the latter is represented by either formula 3 or 3' with (12S,13S,6R,7R)- or (12R,13R,6R,7R)-configurations, because octahydrolaurencin[5] (17) and related compounds with (12S,13R)- or (12R,13S)-configurations gave only the corresponding

debromo (12E)-olefin (15) (IR, 969 $cm^{-1}$) under the same degradation conditions.[9] In view of the splitting pattern (ddd, J = 10, 4, and 2 Hz) due to the proton at C-12 (12-H) (cf., 7-H, ddd, J = 10, 4, and 2 Hz), isolaurepinnacin is assigned reasonably structure 3 rather than 3'.

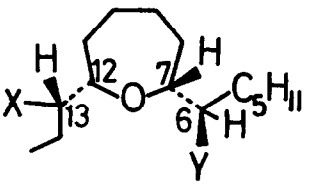
We propose biogenesis shown in Scheme 1 for formation of the metabolites in vivo, which involves a new precursor, (3E,6Z,9Z,12Z)-pentadeca-3,6,9,12-tetraen-1-yne[10] (18), rather than laurediol[3] (1) with (12E)-configuration, and assumes addition of halogen cations[11] to the double bonds.



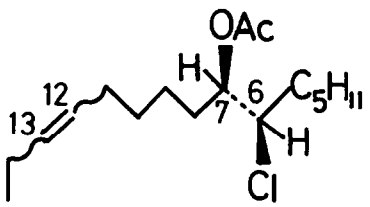
4



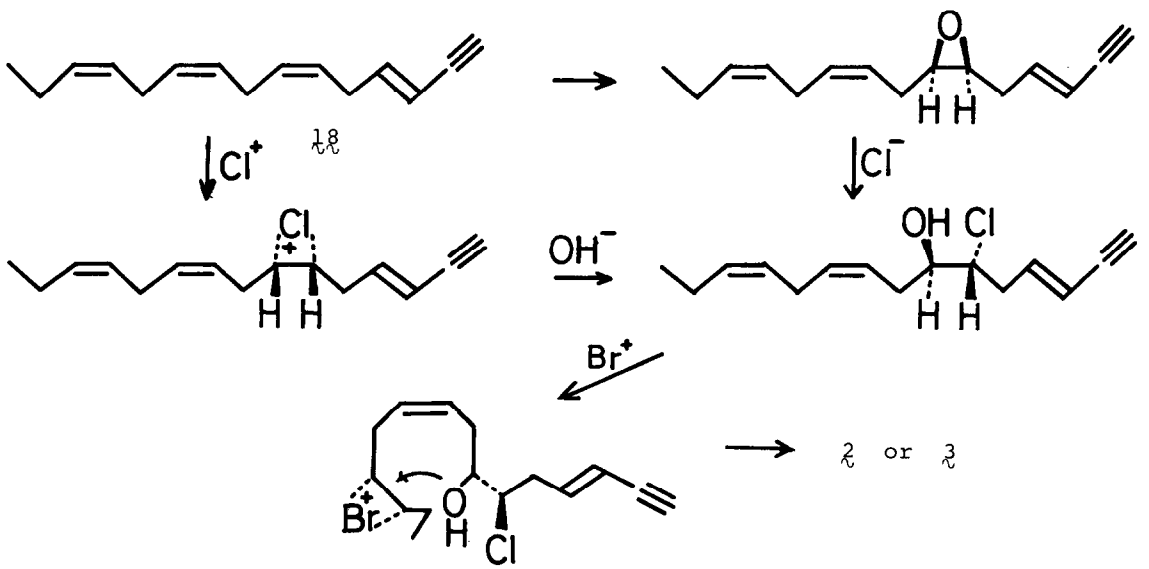
5 $X_1$=Br, $X_2$=H, Y=Cl
6≡10 $X_1$=$X_2$=H, Y=Cl
7≡11 $X_1$=$X_2$=Y=H
8 $X_1$=H, $X_2$=Br, Y=OH
9 $X_1$=H, $X_2$=Br, Y=Cl
12 $X_1$=$X_2$=H, Y=OH
17 $X_1$=H, $X_2$=Br, Y=OAc



13 X=Br, Y=Cl
14 X=Y=H



15 (12E)
16 (12Z)



Scheme 1

## References and Notes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4. All new compounds gave satisfactory spectral data (MS, IR, and $^1$H NMR).
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6. 2: δ ($CDCl_3$) 0.89 (3H, t, J = 7.5, 15-H), 1.54 (1H, ddq, J = 14, 6, and 7.5, 14-H), 1.74 (1H, ddq, 14, 7, and 7.5, 14-H), 2.32 (1H, ddd, J = 14, 8, and 1, 8-H), 2.50 (1H, dddd, J = 15, 10, 7, and 1.5, 5-H), 2.56 (1H, m, 8-H), 2.65 (1H, ddd, J = 12, 6, and 5, 11-H), 2.80 (1H, dddd, J = 15, 7, 4, and 1.5, 5-H), 2.86 (1H, dd, J = 2 and 0.5, 1-H), 3.12 (1H, ddt, J = 10, 1.5, and 12, 11-H), 3.49 (1H, ddd, J = 7, 6, and 2, 13-H), 3.51 (1H, ddd, J = 10, 4, and 1, 7-H), 3.97 (1H, dt, J = 10 and 4, 6-H), 4.10 (1H, ddd, J = 12, 5, and 2, 12-H), 5.61 (1H, ddt, J = 16, 2, and 1.5, 3-H), 5.70 (1H, ddt, J = 6, 2, and 10, 10-H), 5.90 (1H, ddt, 8, 1.5, and 10, 9-H), and 6.29 (1H, ddt, J = 16, 0.5, and 7, 4-H). 3: δ ($CDCl_3$) 0.94 (3H, t, J = 7, 15-H), 1.85 (1H, ddq, J = 14, 4, and 7, 14-H), 1.98 (1H, ddq, J = 14, 5, and 7, 14-H), 2.30 and 2.36 (each 1H, dddd, J = 15, 4, 3, and 2, 8-H and 11-H), 2.55 (2H, m, 8-H, and 11-H), 2.56 (1H, dddd, J = 15, 9, 7, and 1.5, 5-H), 2.78 (1H, dddd, J = 15, 7, 4, and 1.5, 5-H), 2.83 (1H, dd, J = 2 and 0.5, 1-H), 3.52 and 3.59 (each 1H, ddd, J = 10, 4, and 2, 7-H and 12-H), 3.89 (1H, dt, J = 5 and 4, 13-H), 3.92 (1H, dt, J = 9 and 4, 6-H), 5.59 (1H, ddt, J = 16, 2, and 1.5, 3-H), 5.80 and 5.83 (each 1H, dt, J = 8 and 4, 9-H and 10-H), and 6.27 (1H, ddt, J = 16, 0.5, and 7).
7. 2: δ ($CDCl_3$) 10.3 (q), 28.9, 29.4, 35.5, 36.6 (each t), 58.3, 63.0, 76.8, 81.5 (each d), 81.9 (s), 82.1, 111.8, 129.9, 130.3, and 141.9 (each d). 3: δ ($CDCl_3$) 12.7 (q), 28.0, 32.7, 33.8, 37.6 (each t), 61.3, 63.3, 77.0, 81.2 (each d), 82.0 (s), 82.5, 111.8, 129.0, 129.2, and 142.0 (each d).
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11. e.g., W. Fenical, J. Phycol., 11, 245 (1975).


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