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trans- AND *cis*-LAUREDIOL, UNSATURATED GLYCOLS FROM *LAURENCIA NIPPONICA* YAMADA (1)

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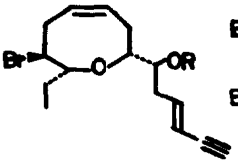
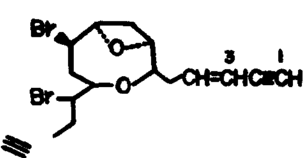
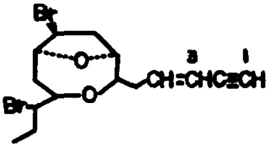
Our extensive studies on the components of *Laurencia nipponica* Yamada and *L. glandulifera* Kützing (Japanese names, Urasozo and Oosozo; Rhodomelaceae) have led to the isolation of a number of cyclic bromoethers with unusual skeletons, laurencin (I) (2), laureatin (II) and isolaureatin (III) (3), laurefucin (IV) and acetyllaurefucin (V) (4), T-laureatin (VI), T-isolaureatin (VII) and deacetyllaurencin (VIII) (5). These ethers have been assumed to be derived biogenetically from a hypothetical precursor, hexadeca-4,7,10,13-tetraenoic acid (IX) or its closely related compounds (6). We now present evidence that, in the alga (*L. nipponica*), such compounds indeed exist as mixture (0.002%) of optical isomers with 6R,7R and 6S,7S configurations of 3-*trans*,9-*cis*,12-*trans*- (Xa and Xb) (7) and 3-*cis*,9-*cis*,12-*trans*-6,7-dihydroxypentadeca-3,9,12-trien-1-yne (XIa and XIb) as well as their diacetates (XIIa∼XIIIb) (0.001%). Each glycol mixture of these optical isomers are designated as *trans*-laurediol and *cis*-laurediol, respectively.



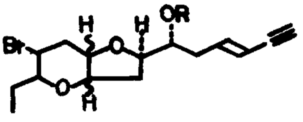
I R=Ac
VIII R=H



II 3-*cis*
VI 3-*trans*



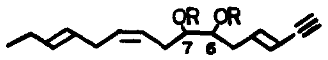
III 3-*cis*
VII 3-*trans*



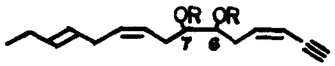
IV R=H
V R=Ac

$CH_3\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH{=}CH\text{-}CH_2\text{-}CH_2\text{-}COOH$

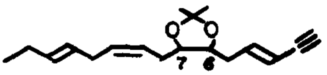
IX



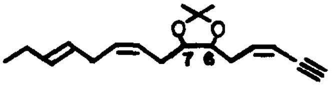
Xa = XIV	R=H	C_6R,C_7R
Xb	R=H	C_6S,C_7S
XIIa=XVI	R=Ac	C_6R,C_7R
XIIb	R=Ac	C_6S,C_7S



XIa	R=H	C_6R,C_7R
XIb=XV	R=H	C_6S,C_7S
XIIIa	R=Ac	C_6R,C_7R
XIIIb=XVII	R=Ac	C_6S,C_7S



XVIIIa=XX	C_6R,C_7R
XVIIIb	C_6S,C_7S



XIXa	C_6R,C_7R
XIXb=XXI	C_6S,C_7S

A laurediol mixture (Xa∼XIb), $C_{15}H_{22}O_2$, colorless oil, $(\alpha)_D$ +19.6° (CCl_4), was obtained by careful chromatography of the methanol extracts of *L. nipponica* Yamada, and showed the following UV and IR absorptions: λ_{max}^{EtOH} 208 (ε 14,900) and 225 nm (18,000), λ_{inf} 219 (ε 16,300) and 233 nm (ε 14,500); ν_{max}^{film} 3400 (OH), 3300 (-C≡CH), 2130 (-C≡C-), 1647 (-CH=CH-), 1630, 1433, 1404, 1056, 968 (*trans* -CH=CH-) and 747 cm^{-1} (*cis* -CH=CH-). The NMR spectrum displayed absorptions of an acetylenic proton at τ 7.30 and 6.97 (1H in total, d, J = 2 Hz), olefinic protons at τ 4.8 - 4.3 (5H, m) and at τ 3.80 (1H, m), allylic protons at τ 8.3 - 7.5 (6H, br. m) and allylic protons flanked by two double bonds and hydroxyl protons around τ 7.18 (4H, br. m), protons on carbons bearing hydroxyl group at τ 6.58 (2H, br. m) and methyl protons at τ 9.02 (3H, t, J = 7), and the MASS spectrum peaks at *m/e* 217, 169 (M^+- C_5H_5), 125 (M^+- C_8H_{13}).

A diacetyllaurediol mixture (XIIa∼XIIIb), $C_{19}H_{26}O_4$ (*m/e* 258 (M^+- AcOH)), $(\alpha)_D$ +14.7°, showed the following absorptions: UV, λ_{max}^{EtOH} 207 (ε 14,500) and 224 nm (ε 17,900), λ_{inf} 218 (ε 15,500) and 232 nm (ε 13,500); IR, ν_{max}^{film} 3280, 2130, 1746, 1650, 1225, 1047, 1027, 965 and 745 cm^{-1}; NMR, τ 9.03 (3H, t, J = 7 Hz), 7.99 (6H, s), 8.3 - 7.2 (8H, m), 7.31 and 6.97 (1H in total, d, J = 2; $-C\equiv C\underline{H}$), 5.08 (2H, m; $2>C\underline{H}$-OAc), 4.8 - 4.4 (5H, m) and 4.02 (1H, m; $-C\underline{H}=CH-C\equiv CH$). Acetylation of (Xa∼XIb) with Ac_2O-Py gave the corresponding diacetate mixture, which was identified as XIIa∼XIIIb in all respects.

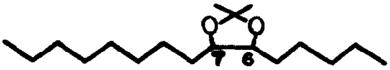
Treatment of deacetyllaurencin (VIII) (2,5), derived from laurencin (I), with Zn-AcOH-EtOH at room temperature gave *trans,cis,trans*-6R,7R-dihydroxy-pentadeca-3,9,12-trien-1-yne (XIV=Xa), unstable colorless crystals, m.p. 26-28°, $C_{15}H_{22}O_2$, $(\alpha)_D$ +27.2°; IR, ν_{max}^{film} 3400, 2130, 1647, 1630, 1433, 1404, 1056, 968 and 747 cm^{-1}; NMR, τ 9.02 (3H, t, J = 7 Hz), 8.3 - 7.5 (6H, br. m; allylic protons), 7.30 (1H, d, J = 2; $-C{\equiv}C\underline{H}$ and 2H, br. m; $-CH{=}CH{-}C\underline{H}_2{-}CH{=}CH{-}$), 6.97 (2H, br. m; 2 -OH), 6.58 (2H, m; 2 $-C\underline{H}OH$), 4.8 - 4.3 (5H, m) and 3.80 (1H, sex. J = 16, 7, 7; $-CH_2{-}C\underline{H}{=}CH{-}C{\equiv}CH$); *m/e* 169 ($M^+$- C_5H_5) and 125 (M^+- C_8H_{13}).

Laureatin (II) (3) was likewise converted into *cis,cis,trans*-6S,7S-dihydroxypentadeca-3,9,12-trien-1-yne (XV=XIb), colorless unstable oil; $C_{15}H_{22}O_2$, (α)$_D$ -19.5°; UV, λ_{max}^{EtOH} 207 (ε 16,600) and 224 nm (ε 18,300), λ_{inf} 217 (ε 16,100) and 232 nm (ε 15,200). The IR spectrum resembled closely that of Xa, except the relative intensities of absorption maxima near 747 cm^{-1} and 970 cm^{-1}.

Careful comparison of the IR and NMR spectra of Xa∼XIb and XIIa∼XIIIb with those of the stereoisomers (XIV and XV) and their diacetates (XVI=XIIa) and (XVII=XIIIb), indicated natural laurediol (Xa∼XIb) to be a *ca.* 1:1 mixture of 3-*trans*- (Xa and Xb) and 3-*cis*-glycol (XIa and XIb). This was supported in the following.

Column chromatography of the acetonides of Xa∼XIb effected the separation of two geometrical stereoisomers; the more polar fractions gave *trans*-acetonide (XVIIIa and XVIIIb), $C_{18}H_{26}O_2$ (M^+ 274), (α)$_D$ +30.0°; IR, ν_{max} 1655, 1630, 1085, 1064 and 967 cm^{-1}; NMR, τ 9.04 (3H, t, J = 7 Hz), 8.71 (6H, s), 7.98 (2H, quin.), 7.35 (1H, d, J = 2) and 3.82 (1H, sex. J = 16, 7, 7); and the less polar *cis*-acetonide (XIXa and XIXb), $C_{18}H_{26}O_2$ (M^+ 274), (α)$_D$ +16.5°; IR, ν_{max} 1655, 1619, 1080, 969, 842 and 754 cm^{-1}; NMR, τ 9.05 (3H, t, J = 7 Hz), 8.71 (6H, s), 8.04 (2H, br. m), 7.04 (1H, d, J = 2) and 3.91 (1H, sex. J = 10, 7, 7). The IR, NMR and MASS spectra of acetonides (XVIIIa and XVIIIb) and (XIXa and XIXb) were superimposable over those of acetonides (XX=XVIIIa and XXI=XIXb) prepared from XIV and XV, respectively. However, their optical rotations were different. Thus, (XVIIIa and XVIIIb), (XIXa and XIXb), XX and XXI were hydrogenated over PtO_2 to eliminate the complexity due to the geometrical isomers and gave the respective saturated acetonides (XXIIa and XXIIb), (XXIIIa and XXIIIb), (XXIV=XXIIa) and (XXV=XXIIIb), which showed the optical rotation, (α)$_D$, of +20.2°, +14.8°, +34.5° and -35.0°, respectively.

Acetonides (XXIV) and (XXV), which possessed *threo* configuration at C_6 and C_7 and were therefore enantiomers each other (2,3), displayed a sharp singlet



XXIIa = XXIV	C_6R,C_7R
XXIIb	C_6S,C_7S
XXIIIa	C_6R,C_7R
XXIIIb = XXV	C_6S,C_7S
XXVI	C_6R,C_7S or C_6S,C_7R

(6H) due to two geminal methyl protons at τ 8.71 in the respective NMR spectrum, while an acetonide (XXVI), which was derived from laurefucin (IV) and possessed erythro configuration (4), exhibited two singlets (each 3H) at τ 8.81 and 8.72. Since the acetonides (XXIIa and XXIIIb) in question exhibit only one sharp singlet (6H) at τ 8.71, threo configuration (RR or SS) must be assigned to each of these acetonides (XXIIa, XXIIIb). On the basis of their optical rotations, the acetonide (XXIIa and XXIIb) is a 4:1 mixture of 6R,7R- (a) and 6S,7S-threo isomers (b) and that (XXIIIa and XXIIIb) a 7:3 mixture. Hence trans-laurediol is a 4:1 mixture of (6R,7R)- and (6S,7S)-3-trans,9-cis,12-trans-6,7-dihydroxypentadeca-3,9,12-trien-1-yne, and cis-laurediol a 7:3 mixture of the corresponding (6R,7R)- and (6S,7S)-3-cis isomers.

References

(1) Part XX of "Constituents from Marine Plant". Part XIX, ref. 4.

(2) T. Irie, M. Suzuki and T. Masamune, Tetrahedron, 24, 4193 (1968).

(3) T. Irie, M. Izawa and E. Kurosawa, Tetrahedron, 26, 851 (1970).

(4) A. Fukuzawa, E. Kurosawa and T. Irie, Tetrahedron Letters, 3 (1972).

(5) T. Irie, A. Fukuzawa, M. Izawa and E. Kurosawa, unpublished data.
T-laureatin (VI): τ 7.18 (1H, d, J = 2 Hz), 4.48 (1H, dd, J = 16, 2).
T-isolaureatin (VII): τ 7.17 (1H, d, J = 2 Hz), 4.48 (1H, dd, J = 15, 2).

(6) Professor Sir Ewart Jones suggested that laurencin was derived (via epoxides) from IX which was found in the algae, (a) Chemistry in Britain, 1966 (2), 6. (b) private communication.

(7) The letters "a and b" in compound numbers, e.g. Xa, in this context denote "6R,7R- and 6S,7S- configurations," respectively.