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LAUREFUCIN AND ACETYLLAUREFUCIN, NEW BROMO COMPOUNDS FROM LAURENCIA NIPPONICA YAMADA (1)

Akio Fukuzawa, Etsuro Kurosawa and Toshi Irie
Department of Chemistry, Faculty of Science, Hokkaido University,
Sapporo, Japan

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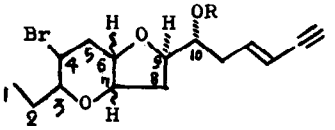
An extensive study of the neutral essential oil from Laurencia nipponica Yamada (Rhodomelaceae; Urasozo in Japanese)(2) led to isolation of a new bromo alcohol and its acetate in 0.02 and 0.0005% yields, respectively. They are designated as laurefucin and acetyllaurefucin and are assigned structures I and II on the basis of the chemical and spectral evidence described below.

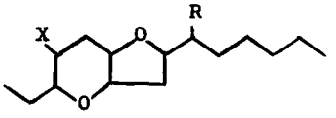
Laurefucin (I), m.p. 107-108°, $[\alpha]_D$ -80°, m/e 265 and 263 ($M^+ - C_5H_5$), was analyzed for $C_{15}H_{21}O_3Br$. The UV (λ_{max} 224.5 nm (ε 17,900), λ_{inf} 232 (14,100)) and IR spectra (ν_{max} 3590, 3400, 3280, 2120, 1629, 1153, 1118, 1100, 1065, 1037, 1020, 965, 879 cm^{-1}) showed the presence of OH, conjugated enyne and ether functions. The NMR spectrum displayed signals due to an acetylenic proton at τ 7.18 (1H, d, J=2 Hz), two vinyl protons at τ 3.76 (1H, dt, J=16, 7, 7) and 4.45 (1H, finely splitted d, J=16), and methyl protons at τ 9.04 (3H, sharp t, J=7). In addition, unresolvable six-proton multiplet appeared in the region of τ 6.6-5.7, which is ascribed to protons on carbons bearing Br, OH and ether oxygen. Acetylation of I gave the corresponding acetate (II), $C_{17}H_{23}O_4Br$, oil, $[\alpha]_D$ -126.5°; m/e 372 and 370 (M^+), 312 and 310 (M^+ - AcOH), 307 and 305 ($M^+ - C_5H_5$); λ_{max} 224.5 nm (ε 16,900), λ_{inf} 232 (13,400); ν_{max} 3280, 2120, 1735, 1628, 1240, 1157, 1097, 1070, 1023, 960 cm^{-1}; τ 9.02 (3H, t, J=7), 7.99 (3H, s), 7.32 (1H, d, J=2.5), 6.55 (1H, dt, J=9, 9, 2), 6.23 (2H, m), 5.96 (1H, br. s), 5.84 (1H, dd, J=7, 4), 5.28 (1H, dt, J=5, 4, 4; >CH-CHOAc-CH_2-), 4.49 (1H, f. split. d, J=16), 3.87 (1H, dt, J=16, 7, 7), which was identified as acetyllaurefucin isolated from the original essential

oil. Laurefucin was, therefore, shown to be a bicyclic ether having $-CH_2-CH_3$, $-CH_2-CH\overset{t}{=}CH-C\equiv CH$, $>CH-CHOH-CH_2-$, and $>CHBr$ groupings and these were further supported by the following experiments.

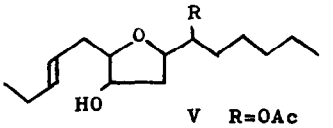
I consumed 3 moles of H_2 over PtO_2 in ethanol to give hexahydrolaurefucin (III), $C_{15}H_{27}O_3Br$, m.p. 63.0-63.5°, $[\alpha]_D$ -53.9°; m/e 318 and 316 ($M^+ - H_2O$); ν_{max} 3600, 3400, 1100, 1065, 1038 cm^{-1}. The NMR spectrum exhibited two methyl signals at τ 9.10 (3H, br.t) and 9.06 (3H, sharp t, J=7), while the original signals due to acetylenic and olefinic protons disappeared.



I R=H
II R=Ac



III R=OH, X=Br
IV R=OAc, X=Br
VI R=OH, X=H
VIII R=X=Br



V R=OAc
XIX R=Cl

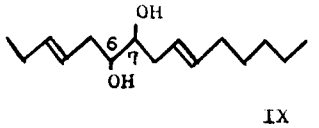
$CH_3-CH_2-CH(O-)-CHBr-CH_2-$ VII

Treatment of hexahydroacetyllaurefucin (IV), acetate of III, with Zn-AcOH yielded an unsaturated acetoxy alcohol (V), $C_{17}H_{30}O_4$ (M^+ 298). The IR and NMR spectra showed that V had $-CH_2-CH\overset{t}{=}CH-CH_2-$ [ν 970 cm^{-1}; τ 4.63 and 4.50 (each 1H, sex, J=16, 6, 6): ABX_2-type), $>CH-CHOH-CH_2-$ [ν 3460 cm^{-1}; τ 6.56 (1H, dt, J=7, 7, 3)], $>CH-CHOAc-CH_2-$ [ν 1745 cm^{-1}; τ 5.21 (1H, dt, J=7, 7, 4) and 7.97 (3H, s)], $>CH-O-CH<$ [ν 1090 cm^{-1}; τ 6.10 (2H, m)], and two methyl groups [τ 9.09 (3H, br.t) and 9.04 (3H, t, J=7)]. The mass spectrum showed the presence of C_5H_9 group [m/e 229 ($M^+ - C_5H_9$), 151 ($M^+ - C_5H_9 - H_2O$- AcOH), 69 (C_5H_9)].

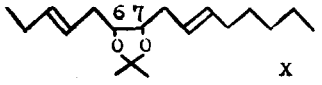
Debromination of III with Raney-Ni afforded hexahydrodebromolaurefucin (VI), $C_{15}H_{28}O_3$ (M^+ 256) which showed sharp triplet (J=7) of methyl signal at τ 9.11 and characteristic peaks due to C_2H_5 group [m/e 227 ($M^+ - C_2H_5$), 209 ($M^+ - C_2H_5 - H_2O$)] in the NMR and mass spectra. Therefore, the partial structure VII is involved in I.

Next, III was treated with $SOBr_2$ in ether at room temp. to give a dibromo compound (VIII), $C_{15}H_{26}O_2Br_2$, m/e 400, 398, 396 (M^+), 371, 369, 367 ($M^+ - C_2H_5$), 237 (M^+- Br- HBr), 221, 219 ($C_9H_{16}OBr$), 179, 177 ($C_6H_{10}OBr$), 139 ($C_9H_{15}O$), 97 (C_6H_9O); τ 9.12 (3H, br.t), 9.04 (3H, t, J=7), 7.94 (1H, m), 7.74 (2H, m), 7.42 (1H, quintet), 6.4-5.8 (6H, m: 2 $>C\underline{H}Br$, 4 $>C\underline{H}-O-$). Four-proton signals in the region of τ 8.0-7.4 in the NMR spectrum could be attributed to those of

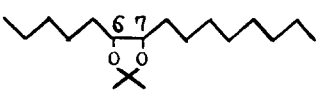
-O-Ċ-C<u>H</u>$_2$-Ċ-Br and/or -O-Ċ-C<u>H</u>$_2$-Ċ-O- (2). On treatment with Zn-AcOH, VIII gave a crystalline unsaturated glycol (IX), $C_{15}H_{28}O_2$, m.p. 94-95°, ν_{max} 3570, 1046, 977 cm^{-1}; τ 9.13 (3H, br.t), 9.03 (3H, t, J=7), 8.74 (6H, br.s), 8.2-7.6 (10H, m), 6.46 (2H, f. split. quintet), 4.54 (4H, m). Acetonide (X) of this glycol exhibited signals due to four olefinic protons at τ 4.61 (m), two protons on carbons attached to oxygen atom at τ 6.08 (quintet), and eight allylic protons at τ 7.69. This spectrum suggested the molecule to constitute a nearly symmetrical structure. The mass spectrum of X displayed characteristic peaks at <u>m/e</u> 265 (M^+- CH_3). 211 (M^+- C_5H_9), 169 (M^+- C_8H_{15}), 111 (C_8H_{15}), 69 (C_5H_9). Hydrogenation of X afforded a saturated acetonide (XI), $C_{18}H_{36}O_2$, $(\alpha)_D$ +4.2°. The mass spectrum (<u>m/e</u> 269 (M^+- CH_3), 227 (M^+- C_3H_5O), 213 (M^+- C_5H_{11}), 171 (M^+- C_8H_{17})) was consistent with the structure XI (3). This acetonide (XI) is very similar to XII from laurencin (2,4) and XIII from laureatin (2) in the mass spectra, but is slightly different in the IR and NMR spectra. Consequently, in view of their optical rotations, the stereochemistry at C_6 and C_7 of XI should be represented by R,S or S,R.



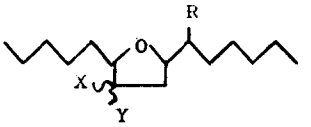
IX



X



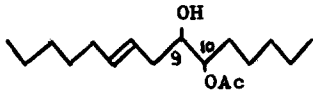
XI $(\alpha)_D$ +4.2°
XII $(\alpha)_D$ +34.5°(C_6R,C_7R)
XIII $(\alpha)_D$ -35.0°(C_6S,C_7S)



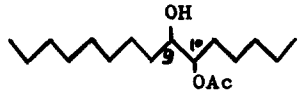
XIV R= OAc, X= Br, Y= H
XX R = Y= H, X= OH
XXI R= H, XY= O

On the other hand, hydrogenation of V followed by treatment with $SOBr_2$ in dioxane at room temp. afforded an acetoxy bromo ether (XIV), $C_{17}H_{31}O_3Br$, ν_{max} 1745, 1230, 1082, 1062, 1026 cm^{-1}; τ 7.99 (3H, s), 6.4-6.0 (3H, m), 4.87 (1H, septet); <u>m/e</u> 223 (M^+- Br- AcOH), 139 ($C_9H_{15}O$). Treatment of XIV with Zn-AcOH yielded an unsaturated acetoxy alcohol (XV), $C_{17}H_{32}O_3$, ν_{max} 972 cm^{-1}; τ 6.54 (1H, m), 5.33 (1H, sextet), 4.66 (2H, m); <u>m/e</u> 266 (M^+- H_2O). Hydrogenation of XV gave a saturated acetoxy alcohol (XVI), $C_{17}H_{34}O_3$, $(\alpha)_D$ +22°, ν_{max} 3440, 1744 cm^{-1}; τ 9.11 (6H, br.t), 7.99 (3H, s), 6.60 (1H, br.m), 5.35 (1H, f. split. quartet), which was identical with the specimen derived from laurencin ((i) H_2/PtO_2 (ii) Zn-AcOH (iii) H_2/PtO_2) in all respects. While the IR and NMR spectra of XVI were very similar as those of XVII ($(\alpha)_D$ -20.3°) derived

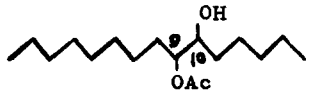
from laureatin [(i) H_2/PtO_2 (ii) KOH-EtOH (iii) Zn-AcOH (iv) Ac_2O (v) H_2/Pd-C], the mass spectrum of XVI differed definitely from that of XVII. The position and stereochemistry of >CH-OH group and one (C_9) of the carbons bearing ether oxygen in I were thus established unambiguously and, therefore, the whole skeleton of laurefucin could be represented by XVIII.



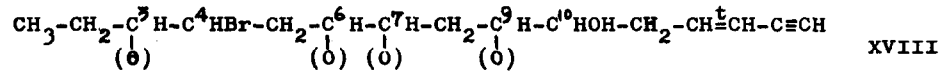
XV



XVI ($C_9R, C_{10}R$)



XVII ($C_9S, C_{10}S$)



XVIII

Since it is clear that laurefucin contains neither oxirane nor oxetane ring on the chemical and spectral data mentioned above, I is the most favorable structure for laurefucin.

Finally, the oxolane ring in I has been confirmed by the following experiments. XIX, $C_{15}H_{27}O_2Cl$ (M^+ 276, 274), obtained from III [(i) $SOCl_2$ (ii) Zn-AcOH], was treated with H_2/PtO_2 followed by Raney-Ni to give XX, $C_{15}H_{30}O_2$, m/e 171 ($M^+ - C_5H_{11}$), 157 ($M^+ - C_6H_{13}$). XX was then oxidized with Ag_2O in benzene (reflux 48 hr) to yield the corresponding ketone XXI, $C_{15}H_{28}O_2$ (M^+ 240), $[\alpha]_D$ +107.1°; τ 9.09 (6H, br.t), 8.04 and 7.63 (each 1H, J_{AB}=18, J_{AX}=13, J_{BX}=6), 6.42 (1H, br.dd), 6.02 (1H, m). This ketone XXI showed the IR absorptions, ν_{max} 1764, 1164, 1094 cm^{-1}, characteristic of β-keto-oxolane (5).

It is concluded that the structures of laurefucin and acetyllaurefucin are represented by I and II, respectively. Laurefucin, laurencin, laureatin, and isolaureatin (2), all these compounds were isolated from Laurencia species and could be assumed to be derived biogenetically from a common precursor, pentadeca-3,9,12-trien-1-yn-6,7-diol.

References

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