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Structure of Lyoniol-A (Lyoniatoxin)

Lyoniol-A (Lyoniatoxin)[1] $C_{20}H_{27}(OH)_4(OAc)(-O-)$ (I) is the main component of the toxic principles of *Lyonia ovalifolia* DRUDE (SIEB. et ZUCC.) var. *elliptica* HAND.-MAZZ. I was indicated to have four $\geqslant C-CH_3$ and an epoxide $-\overset{H}{\underset{\diagdown}{C}}-\overset{O}{\underset{\diagdown}{}}-\overset{H}{\underset{\diagdown}{C}}-$ from it's nuclear magnetic resonance (NMR) data: $\delta^{C_5H_5N}_{ppm}$ 1.26 (3H, singlet, $\geqslant C-CH_3$), 1.50 (3H, singlet, $\geqslant C-CH_3$), 1.57 (3H, singlet, $-C(OH)-\underline{CH_3}$), 1.88 (3H, broad singlet, $-C(OH)-\underline{CH_3}$), 2.17 (3H, singlet, $OCOCH_3$), 2.89 (1H, broad singlet, $\geqslant C(-C(OH)-H)-\underline{H}$), 3.27 (1H, doublet, J=3.0 cps, $-C(-O-)-\underline{H}$), 3.88 (1H, doublet, J=9.5 cps, $-C(OAc)-\underline{H}$), 4.21 (1H, doublet, J=3.0 cps, $-C(OH)-\underline{H}$), 5.64 (1H, doublet, J=9.5 cps, $-C(AcO)-\underline{H}$). Alkaline hydrolysis of I afforded deacetyl compound $C_{20}H_{27}(OH)_5$ (-O-) (II), NMR $\delta^{C_5D_5N\text{-}D_2O}_{ppm}$: 1.26 (3H, singlet), 1.55 (6H, singlet), 1.85 (3H, singlet), 2.86 (1H, broad singlet), 3.32 (1H, doublet, J=3.0 cps), 3.75, 3.98 (2H, AB quartet, J=9.3 cps), 4.30 (1H, doublet, J=3.0 cps). II was reversed to lyoniol-A with acetic anhydride and pyridine. The deacetyl derivative II consumed one mole of sodium periodate, but I did not, thus the acetoxyl group located vicinal to a hydroxyl group. The NMR data of I and II reveal that the glycolic part of the molecule is inserted between two tertiaryly substituted carbon atoms. The acetonide of II, formed in acetone with *p*-toluenesulfonic acid, is colorless needles from benzene and chloroform mixture (1:1), mp 241—249°. *Anal.* Calcd. for $C_{23}H_{36}O_6$: C, 67.62; H, 8.88. Found: C, 67.79; H, 8.99. NMR $\delta^{C_5D_5N}_{ppm}$ 1.21, 1.44, 1.49, 1.51, 1.62, 1.83 (each 3H, singlet, $\geqslant C-CH_3 \times 6$), 2.85 (1H, broad singlet), 3.32 (1H, doublet, J=3.0 cps), 3.82 (1H, broad doublet, J=*ca.* 9.0 cps), 4.21 (1H, doublet, J=3.0 cps), 4.32 (1H, doublet, J=9.0 cps). This acetonide did not react with chromic acid in pyridine. Therefore three remaining hydroxyl groups are suggested to be tertiary alcohols.

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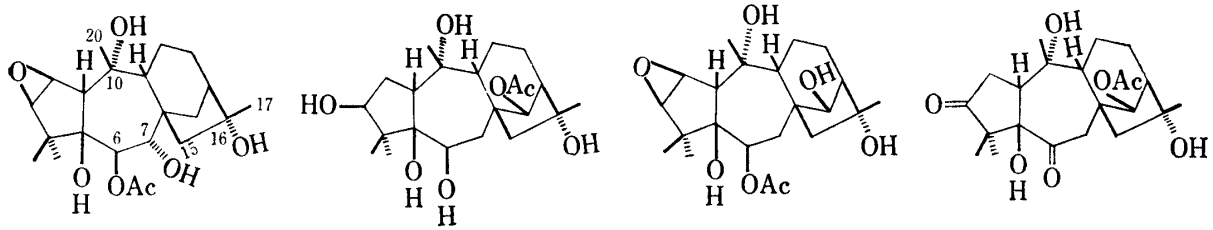
Oxidation of I with chromic acid in pyridine gave a monoketone (III), colorless needles from ethanol, mp 249—250°. *Anal.* Calcd. for $C_{22}H_{32}O_7$: C, 64.68; H, 7.90. Found: C, 64.60; H, 7.99. IR cm^{-1} (KCl): ν_{CH} 3450, ν_{CO} 1740 (acetyl), ν_{CO} 1712, ν_{C-O} 1263. NMR $\delta_{ppm}^{C_5D_5N}$: 1.05, 1.44, 1.63, 1.87 (each 3H, singlet, $\geqslant C-CH_3 \times 4$), 2.10 (3H, singlet, $OCOCH_3$), 3.11 (1H, broad singlet), 3.35 (1H, doublet, $J=3.0$ cps), 4.23 (1H, doublet, $J=3.0$ cps), 5.75 (1H, singlet). III is believed to be a six or more membered ring ketone from it's infrared carbonyl frequency: ν_{CO} 1712 cm^{-1}. From the above NMR data the partial structure of this ketone (III) can be written like this: $\geqslant C-\underset{\underset{OAc}{|}}{\overset{\overset{H}{|}}{C}}-\!\!-C-C\leqslant$ (O).



I X XI XII

Fig. 1

Reduction of I with lithium aluminum hydride yielded a hexaalcohol (IV): colorless needles from ethyl acetate, mp 173—187°. *Anal.* Calcd. for $C_{20}H_{34}O_6$: C, 64.84; H, 9.25. Found: C, 64.51; H, 9.00. Triacetate (V): colorless needles from ethyl acetate, mp 219.5—222°. NMR $\delta_{ppm}^{CDCl_3}$ 0.99, 1.06, 1.36, 1.59 (each 3H, singlet, $\geqslant C-CH_3 \times 4$), 1.98 (3H, singlet, $OCOCH_3$), 2.09 (6H, broad singlet, $OCOCH_3 \times 2$), 4.83 (1H, doublet like, $J=ca.$ 5.0 cps), 5.13, 5.30 (2H, AB quartet, $J=10.8$ cps). By these results was verified the fact that the epoxide ring was converted into a hydroxide. Acetylation of I with acetic anhydride and pyridine at higher temperature afforded a pentaacetate, colorless needles from ether, mp 191.5—194.5°, which has no epoxide ring proton signal at 3.29—4.21 ppm in NMR chart. NMR $\delta_{ppm}^{CDCl_3}$ 1.02, 1.14, 1.45, 1.55 (each 3H, singlet, $\geqslant C-CH_3 \times 4$), 1.95, 2.03, 2.04, 2.09, 2.11 (each 3H, singlet, $OCOCH_3 \times 5$), 2.68 (1H, doublet, $J=4.0$ cps), 4.78 (1H, singlet), 5.12, 5.21 (2H, AB quartet, $J=9.0$ cps), 5.47 (1H, doublet, $J=4.0$ cps). This result indicated that the epoxide ring was opened and formed two acetoxyl groups.

IV was treated with *p*-toluenesulfonic acid in acetone at room temperature to yield a monoacetonide (VI) and two monodehydro monoacetonide derivatives (VII) and VIII. VI: colorless prisms from hexane, mp 194—196.5°. NMR $\delta_{ppm}^{CDCl_3}$: 1.01 (3H, singlet), 1.20 (3H, singlet), 1.38 (12H, singlet, $\geqslant C-CH_3 \times 4$), 3.59, 3.77 (2H, AB quartet, $J=9.0$ cps), 3.5—3.7 (1H, triplet like, $J=ca.$ 6.0 cps). VII: colorless needles from hexane, mp 200—211°. *Anal.* Calcd. for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.71; H, 9.20. IR cm^{-1} ($CHCl_3$): $\nu_{C=C}$ 1630. NMR $\delta_{ppm}^{CDCl_3}$: 1.03, 1.21, 1.37 (each 3H, singlet, $\geqslant C-CH_3 \times 3$), 1.39 (6H, singlet, $\geqslant C-CH_3 \times 2$), 3.64 (1H, triplet, $J=4.0$ cps), 3.71, 3.79 (2H, AB quartet, $J=9.0$ cps), 5.02 (1H, broad singlet, $>C=C<\underset{H}{\overset{H}{}}$), 5.15 (1H, broad singlet, $>C=C<\underset{H}{\overset{H}{}}$). VIII: colorless needles from acetone, mp 182—183°. *Anal.* Calcd. for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.08; H, 9.28. IR cm^{-1} ($CHCl_3$): $\nu_{C=C}$ 1675. NMR $\delta_{ppm}^{CDCl_3}$: 1.30 (6H, singlet, $\geqslant C-CH_3 \times 2$), 1.33, 1.37, 1.44 (each 3H, singlet, $\geqslant C-CH_3 \times 3$), 1.95 (3H, broad singlet, $HC\equiv C-C\underline{H}_3$), 3.83 (1H, triplet, $J=4.0$ cps), 4.37, 4.60 (2H, AB quartet, $J=6.2$ cps), 4.8—5.0 (1H, multiplet, $\geqslant C-\underset{\underset{H}{|}}{C}=C<\underset{CH_3}{}$). VII gave a cyclopentanone derivative (IX) with chromic acid oxidation in pyridine. IX: colorless needles from hexane, mp 178—178.5°. *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found:

C, 70.38; H, 8.78. IR cm^{-1} ($CHCl_3$): ν_{CO} 1752. NMR $\delta_{ppm}^{CDCl_3}$ 1.12, 1.18 (each 3H, singlet, $\geqslant C-CH_3 \times 2$), 1.38 (6H, singlet, $\geqslant C-CH_3 \times 2$), 1.40 (3H, singlet, $\geqslant C-CH_3$), 3.87 (2H, singlet, $\geqslant C-\underset{O}{\overset{H}{C}}-\underset{O}{\overset{H}{C}}-C\leqslant$), 4.92 (1H, broad singlet, $>C=C<^{H}_{H}$), 5.14 (1H, broad singlet, $>C=C<^{H}_{H}$).

This result proves that the epoxide group is situated on a cyclopentane ring.

Lyoniol-A seems to have the same carbon skeleton and a very similar stereostructure as grayanotoxin-I(X)[2] and rhodojaponin-II (XI)[3] because of a close relationship between the plant sources (toxic species of ericaceous family) and similar biological activity. Thus the structure of lyoniol-A should be represented by formula I. From the coupling constant of C_6–H and C_7–H and speculation about stereomodels we concluded that C_6–H, C_7–H are *trans* and, therefore the C_7-hydroxyl group must be α-configuration. The structures of VII and VIII supposed to be $\Delta^{10,20}$-ene-6,7-acetonide(vinyl protons) and $\Delta^{15,16}$-ene-6,7-acetonide-(allyl coupling of 17-methyl) respectively. Deacetyl derivative of I was thought to consume two moles of sodium periodate, but experiment resulted only one mole under a same condition as quinic acid consumed two moles of periodate. The grayanotoxin diketoderivative(XII)[4] consumes no periodate. Between this fact and resistance of lyoniol-A against sodium periodate there seems to be some relation ship. Further study is in progress.

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Structure of Innovanoside

A new glycoside, innovanoside, was isolated from the leaves of *Evodiopanax innovans* NAKAI (Araliaceae) as one of minor glycosidic constituents. The methanol extract of the leaves was concentrated, diluted with water, and the resinous precipitate was removed. The aqueous solution was extracted with ethyl acetate, the extract was dissolved in methanol–ethyl acetate and chromatographed on silica gel column. The eluate was rechromatographed on silica gel with chloroform–methanol mixture. From the main fraction yielded a white powder (innovanoside)(I), mp 122—128°, $[\alpha]_D^{15}$ −132° (c=1.1, methanol).[1] NMR $\delta_{ppm}^{d_6\text{-DMSO}}$: 2.34 (3H, singlet, $=\overset{|}{C}-C\underline{H}_3$), 4.3—5.6 (6H, broad, sugar hydrogen), 6.35 (1H, doublet, J=5.5

1) Melting points are uncorrected. Optical rotations were determined on a OR-10 spectrometer (Yanagimoto). NMR spectra were determined on a JNM-MH-60 spectrometer (Japan Electron Optics Lab. Tokyo Japan). Tetramethylsilane as internal standard.