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Sesquiterpenes from *Dictyopteris Divaricata.* II.[1] Dictyopterol and Dictyopterone

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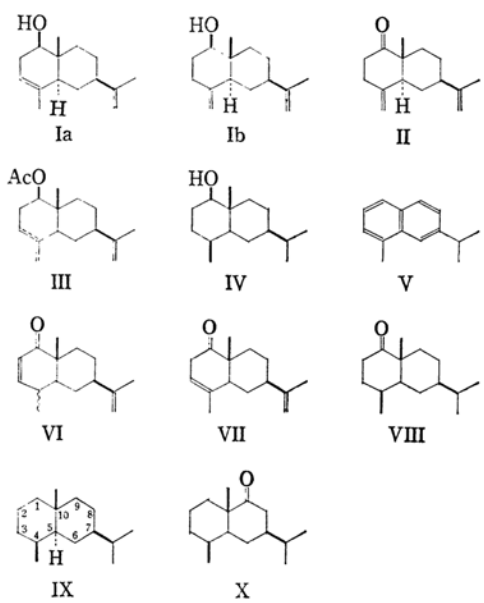
The structures of new sesquiterpenes, dictyopterol and dictyopterone, isolated from the essential oil of a brown algae, *Dictyopteris divaricata* Okamura ("Yezoyahazu"), have been shown to be selinen-1β-ol and selinen-1-one, respectively, on the basis of chemical and spectral data. Dictyopterol is an inseparable mixture of α- and β-isomers.

During the course of a search on the sesquiterpenes from the essential oil of *Dictyopteris divaricata* Okamura, a sesquiterpene alcohol has been isolated.[2] The present paper is concerned with the structural elucidation of the alcohol and also of a new ketone isolated during the studies. On the basis of the experimental evidence described below, the alcohol, designated dictyopterol (I), and the ketone, dictyopterone (II), are shown to be selinen-1β-ol and selinen-1-one, respectively.

Dictyopterol (I), $C_{15}H_{24}O$, $[\alpha]_D^{22}$ $-30.8°$, was obtained in ca. 0.12% yield from the neutral fraction of the essential oil of the seaweed. The infrared spectrum indicated the presence of a secondary hydroxyl group at ν 3400 and 1038 cm^{-1} and terminal methylene groups at ν 1642 and 888 cm^{-1}. The NMR spectra measured at 60 and 100 Mc. showed a signal due to an olefinic methyl group at τ 8.25 and two sharp peaks at τ 9.31 and 9.23. The latter peaks altogether involved three protons and the ratio of the intensity of the respective peaks was about 3 : 2. A broad signal due to an olefinic proton, centered at τ 4.7, appeared besides two peaks due to the terminal methylene protons at τ 5.47 and 5.29. However, the intensity of the absorption at lowest field was equivalent to only about 0.4 proton. Similar signals were observed in the NMR spectrum of dictyopterol acetate (III), obtained by acetylation of I with acetic anhydride in pyridine. These NMR spectral data suggested that the alcohol was probably a mixture (about 2 : 3) of structural isomers caused by the different disposition of a double bond, i. e., α- (Ia) and β-dictyopterol (Ib); the peaks in the high field were attributable to a tertiary methyl group. This inference was supported by hydrogenation and the oxidation experiments. The catalytic hydrogenation of dictyopterol acetate (III) over Adams' catalyst in acetic acid followed by hydrolysis gave quantitatively tetrahydrodictyopterol (IV), $C_{15}H_{28}O$, which was shown to be a single compound in all respects. This saturated alcohol should be bicyclic and showed in its NMR spectrum the presence of a secondary methyl group at τ 9.21, a tertiary methyl group at τ 9.17, and an isopropyl group at τ 9.12. Selenium dehydrogenation of III gave eudalene (V), suggesting that IV possessed a selinane skeleton, a view that was confirmed later.

Oxidation of I with chromium trioxide in pyridine afforded a mixture of two isomeric ketones, $C_{15}H_{22}O$, which were separated by chromatography. One of these ketones was identical with dictyopterone (II), isolated from the essential oil, and the other was an α, β-unsaturated ketone (VI), λ 227 mμ



1) Part V of "Constituents from Marine Plants"; Part IV, T. Irie, M. Suzuki, E. Kurosawa and T. Masamune, *Tetrahedron Letters*, **1966**, 1837.

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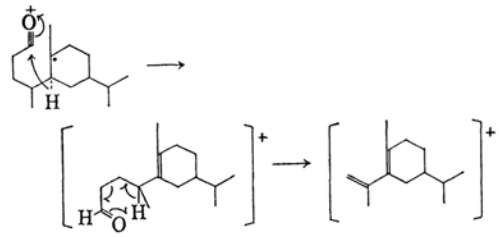
2) T. Irie, K. Yamamoto and T. Masamune, This Bulletin, **37**, 1053 (1964).

(log ε 4), ν 1680 cm^{-1}. Since only a small amount of the latter was available, no chemical investigation could be carried out. However, neither α- nor β-dictyopterol was characterized as an allylic alcohol. Hence, this α, β-unsaturated ketone was probably formed by migration of a double bond from a β, γ-position, i. e., VII.

Dictyopterone (II), $C_{15}H_{22}O$, $[\alpha]_D^{21}$ −12.5°, was newly isolated from the neutral fraction of the essential oil beside I and was also obtained by the oxidation of I as mentioned above. The infrared spectrum showed the presence of a six-membered ring carbonyl (ν 1710 cm^{-1}) and terminal methylene group (ν 1640, 890 cm^{-1}). The NMR spectrum indicated the presence of two terminal methylene groups at τ 5.34 and 5.07 (total 4H), a methyl group on an olefinic carbon at τ 8.28, and a tertiary methyl group at τ 9.05. This unsaturated ketone II was stable toward alkali, indicating that the double bond is not located at a β, γ-position relative to the carbonyl group. When II was reduced with lithium aluminum hydride in tetrahydrofuran, a corresponding alcohol was obtained, the NMR spectrum of which showed a sharp singlet at τ 9.31 (3H), a doublet (J=2 c. p. s.) at τ 8.25 (3H), and broad peaks at τ 5.47 and 5.29 (total 4H). It was found that this alcohol was identical with one of the components of I, i. e., β-dictyopterol (Ib), by comparisons of the infrared and NMR spectra of this alcohol and I.

Catalytic hydrogenation of II yielded tetrahydrodictyopterone (VIII), $C_{15}H_{26}O$, which was also obtained by the chromium trioxide oxidation of IV; VIII displayed positive Zimmermann test. Treatment of VIII with heavy water in the presence of sodium deuteroxide in dioxane afforded a dideuterio derivative (mass spectrum: *m/e* 224). The ketone therefore has $-CH_2-CO-\dot{C}(\dot{C})-C$ grouping.

The Wolff-Kishner reduction of VIII gave (+)-selinane (IX); this transformation has now established the carbon skeleton as well as the stereochemistry of the tertiary methyl and the isopropyl group in VIII, and tetrahydrodictyopterone should therefore be selinan-1-one (VIII). The alternative structure X (selinan-9-one) is ruled out because the α, β-unsaturated ketone VI was formed by the oxidation of I and because tetrahydrodictyopterone showed the infrared spectrum different from that of dihydrocanarone[3] (X). Optical rotatory dispersion curves of II and VIII showed small positive and samll negative Cotton effects, respectively. Furthermore, the mass spectra of both VIII and its dideuterio derivative showed a remarkable peak at *m/e* 178 which was formulated as follows, supporting the structure of VIII.

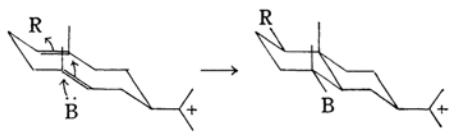


m/e 178

Finally, the conformation of the hydroxyl group in I is equatorially disposed and, therefore, β-oriented because tetrahydrodictyopterol acetate showed in its NMR spectrum a broad multiplet (half-band width ca. 16 c. p. s.) at τ 5.6 attributable to an axial hydrogen on a carbon bearing the acetoxyl group.

All the facts discussed above show that Ia, Ib, and II are the most favorable structures for α- and β-dictyopterols and dictyopterone, respectively.

These 1-oxygenated selinenes may be considered to be formed biogenetically as a result of *trans*-anti-parallel oxidative cyclization of a germacrane-type intermediate XI.[4]



XI

Experimental

The melting points are uncorrected. The ultraviolet and infrared spectra were measured using a Hitachi spectrophotometer and a Nippon Bunko 402-G or IR-S spectrophotometer, respectively. The NMR measurements were performed in carbon tetrachloride with a Nippon Denshi 60-Mc. spectrophotometer using tetramethylsilane as an internal reference unless otherwise stated. The ORD and mass spectra were measured with a Nippon Bunko ORD/UV-5 and a Hitachi RMU-6 mass spectrometer, respectively.

The Isolation of Dictyopterol (I) and Dictyopterone (II).—a) The neutral fraction[2] of the essential oil from *D. divaricata* was submitted to distillation in vacuo; after removal of fractions up to b. p. 106.5°C/4 mmHg, the residual oil (14 g.) was chromatographed on silica gel containing 20% Celite. The benzene eluate was rechromatographed over neutral alumina, and a mixture of dictyopterol and δ-cadinol was obtained. Repeated chromatography afforded dictyopterol free from δ-cadinol, but a better result was obtained by

3) V. K. Hinge, A. D. Wagh, S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron*, **21**, 3197 (1965); cf. A. D. Wagh, S. K. Paknikar and S. C. Bhattacharyya, *J. Org. Chem.*, **29**, 2479 (1964).

4) Cf. J. B. Hendrickson, *Tetrahedron*, **7**, 82 (1959).

the following treatment. A mixture of dictyopterol and δ-cadinol was treated with acetic anhydride and pyridine, and the crude product was taken up in *n*-hexane and chromatographed over neutral alumina. Elution with *n*-hexane - benzene (3 : 1) yielded dictyopterol acetate (III) (488 mg.) as pure (T.L.C.), colorless oil, $[\alpha]_D^{19}$ −15.5° (*c* 2.0, EtOH); ν_{max}^{film} 3080, 1742, 1642, 1240, 1026, 890 cm^{-1}; NMR: τ 9.25, 9.17 (total 3H, two singlets), 8.29 (more than 3H, doublet, J= 2 c. p. s.), 8.02 (3H, singlet), 5.5 (1H, multiplet), 5.34, 5.28 (total more than 3H, broad multiplets), and 4.8 (ca. 0.4H, broad multiplet).

Found: C, 78.02; H, 10.02. Calcd. for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99%.

The above acetate III (278 mg.) dissolved in a mixture of methanol (50 ml.) and ether (5 ml.) was added to 5% aqueous potassium hydroxide (10 ml.), and the solution was kept aside at room temperature for 2 days. After addition of water and removal of the organic solvent in vacuo, the residue was extracted with ether. The ether extracts were washed, dried and evaporated, giving an oily product which was chromatographed on neutral alumina. Elution with benzene - ethyl acetate (5 : 1) afforded pure (T. L. C.) I as a colorless oil, $[\alpha]_D^{22}$ −30.8° (*c* 2.08, CCl_4); ν_{max}^{film} 3400, 3080, 1642, 1038, 888 cm^{-1}; NMR: τ 9.31, 9.23 (total 3H, two singlets), 8.25 (more than 3H, doublet, J=2 c. p. s.), 6.6 (1H, broad multiplet), 5.47, 5.29 (total more than 3H, broad multiplets), and 4.7 (ca. 0.4H, broad multiplet). Mass spectrum: *m/e* (rel. abund.) 220 (100), 205 (81), 202 (84), 161 (91), 159 (84), 133 (83), 93 (82), 81 (71).

Found: C, 81.47; H, 10.65. Calcd. for $C_{15}H_{24}O$: C, 81.76; H, 10.98%.

The *n*-hexane - benzene (3 : 1) eluate in the chromatography of the residual oil described above, was rechromatographed over neutral alumina, and dictyopterone (II) was obtained (161 mg.), $[\alpha]_D^{21}$ −12.5° (*c* 2.16, CCl_4); ν_{max}^{film} 3080, 1710, 1640, 890 cm^{-1}; NMR: τ 9.05 (3H, singlet), 8.26 (3H, doublet, J=2 c. p. s.), 5.30, 5.07 (total 4H, broad multiplets).

Found: C, 82.73; H, 10.02. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16%.

b) The neutral fraction (25 g.) of the essential oil was chromatographed on neutral alumina and eluted successively with *n*-hexane, benzene, ether, and ethyl acetate. The product (ca. 7 g.) obtained from the eluates with ether and ethyl acetate was distilled with steam. The distillate was extracted with ether and dried. After removal of the solvent, the residual oil was chromatographed on silica gel. Each eluate was treated as described above, yielding I and II.

The Hydrogenation of Dictyopterol Acetate (III).—Dictyopterol acetate (III) (208 mg.) in glacial acetic acid (15 ml.) was hydrogenated over Adams' catalyst (15 mg.) at room temperature until gas absorption ceased (2 mol. of hydrogen was absorbed after 2 hr.). The catalyst was removed by filtration and the solvent was evaporated under reduced pressure. The residual oil was chromatographed on alumina. The fraction eluted with *n*-hexane - benzene (3 : 1) afforded pure (T. L. C.) tetrahydrodictyopterol acetate (196 mg.). ν_{max}^{film} 1742, 1240, 1024 cm^{-1}; NMR: τ 9.12 (9H, doublet, J=6 c. p. s.), 9.08 (3H, singlet), 8.05 (3H, singlet), 5.6 (1H, broad multiplet).

Found: C, 76.95; H, 11.25. Calcd. for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35%.

Tetrahydrodictyopterol (IV).—To a solution of the afore-mentioned tetrahydro-acetate (190 mg.) in a mixture of methanol (20 ml.) and ether (5 ml.) was added 5% aqueous potassium hydroxide (3 ml.), and the mixture was allowed to stand at room temperature for 2 days. After addition of water to the reaction mixture, the organic solvent was removed in vacuo and the residue was extracted with ether. The ether solution was washed with 0.5 N hydrochloric acid, 2% sodium bicarbonate solution, and then with water, successively. Removal of the solvent afforded an oily material, which was chromatographed on alumina. The fraction eluted with benzene - ethyl acetate (5:1) gave pure (T. L. C.) tetrahydrodictyopterol (IV) (136 mg.). ν_{max}^{film} 3400, 1020 cm^{-1}. NMR: τ 9.21 (3H, doublet, J=6 c. p. s.), 9.17 (3H, singlet), 9.12 (6H, doublet, J=6 c. p. s.), 6.9 (1H, broad multiplet).

Selenium Dehydrogenation of Dictyopterol Acetate (III).—A mixture of III (80 mg.) and selenium (85 mg.) was heated in a sealed tube at 282—294°C for 6 hr. The reaction mixture was extracted with ether and the ether extracts were dried. After removal of the solvent, the residue was chromatographed on alumina thin layer using *n*-hexane. The fraction of R_f=1 33 mg.) was identified as eudalene (V), λ_{max}^{EtOH} mμ (ε): 228 (36.700), 282 (3200), 320 (383). ν_{max}^{film} 1630, 1600, 1510, 1380, 1360, 1300, 1170, 1150, 1080, 1042, 878, 830, 750 cm^{-1}.

Picrate: m. p. 87—89°C, yellow needles (from ethanol).

The Oxidation of Dictyopterol (I).—A solution of I (109 mg.) in dry pyridine (5 ml.) was added to a complex of chromium trioxide (300 mg.) and pyridine (3 ml.) and the mixture was set aside at room temperature overnight. The reaction mixture was distilled with steam and the distillate was extracted with ether. The ether extracts were washed with 0.5 N hydrochloric acid, 0.5 N sodium hydroxide solution, then with water and dried. After removal of the solvent in vacuo, the residual oil was chromatographed on alumina. The fraction eluted with *n*-hexane - benzene (3 : 1) afforded pure (T. L. C.) oily product (61 mg.), which was identified as dictyopterone (II) in all respects.

The fraction eluted with benzene gave an α,β-unsaturated ketone (14 mg.). λ_{inf}^{EtOH} 227 mμ (log ε 4). ν_{max}^{film} 1680 cm^{-1}.

The Alkaline Treatment of Dictyopterone (II).—A mixture of II (12 mg.) and 5% methanolic potassium hydroxide was refluxed for 1 hr. After addition of water and removal of the methanol in vacuo, an oily product was extracted with ether and the ether extracts were washed with water and dried. On removal of the solvent, the starting material II was recovered unchanged.

The Reduction of Dictyopterone (II) with Lithium Aluminum Hydride.—To a suspension of lithium aluminum hydride (25 mg.) in dry tetrahydrofuran (10 ml.), a solution of II (59 mg.) in the same solvent (5 ml.) was added and then the mixture was refluxed for 2 hr. After being cooled, the mixture was decomposed by the addition of water and acidified with dilute sulfuric acid. The solution was extracted with ether and the ethereal layer was washed with 2% sodium

bicarbonate solution and then with water and dried. After removal of the solvent, the residual oily product was chromatographed on alumina. The product eluted with benzene - ethyl acetate (5 : 1) was identified as β-dictyopterol (Ib) by a comparison of the infrared and NMR spectra. ν_{max}^{film} 3400, 3080, 1642, 1038, 888 cm^{-1}. NMR: τ 9.31 (3H, singlet), 8.25 (3H, doublet, J=2 c. p. s.), 6.6 (1H, broad quartet), 5.47 and 5.29 (total 4H, broad multiplets).

Tetrahydrodictyopterone (VIII).—Dictyopterone (29 mg.) in glacial acetic acid (6 ml.) was hydrogenated over Adams' catalyst (3 mg.) at room temperature. After 2 hr. the catalyst was removed and the acetic acid solution was neutralized with 5% aqueous potassium hydroxide. The neutral solution was extracted with ether and the ethereal layer was washed with water and dried. Removal of the solvent afforded an oily product, which was chromatographed on alumina. The fraction eluted with benzene gave oily saturated ketone VIII (22 mg.). $[\alpha]_D^{22}$ −41.6° (c 1.01, MeOH). The ultraviolet spectrum showed only an end absorption. ν_{max}^{film} 1705, 1390, 1372, 1285, 1140, 1077, 1010, 916 cm^{-1}. NMR: τ 9.12 (6H, doublet, J=6 c. p. s.), 8.92 (3H, singlet), 8.92 (3H, doublet, J=7 c. p. s.). Mass spectrum: *m/e* (rel. abund.) 222 (92), 220 (92), 178 (98), 135 (79), 109 (74), 81 (81), 43 (100).

The Oxidation of Tetrahydrodictyopterol (IV).—The oxidation of IV (110 mg.) with chromium trioxide was carried out as described in the case of I, yielding a crude oily product which was chromatographed over alumina. The fraction eluted with *n*-hexane - benzene (3 : 1) was identified as tetrahydrodictyopterone (VIII) obtained by the catalytic hydrogenation of II.

The Wolff-Kishner Reduction of Tetrahydrodictyopterone (VIII).—To a solution of sodium (250 mg.) in diethylene glycol (7 ml.), VIII (45 mg.) in the same solvent (3 ml.) and 100% hydrazine hydrate (1.3 ml.) were added, and the mixture was heated at 180—185°C for 20 hr. After addition of water, the mixture was extracted with ether. The ether extracts were washed with water, dried and the ether was removed in vacuo. The oily product thus obtained was chromatographed on alumina. The fraction eluted with *n*-hexane afforded a colorless oil, $[\alpha]_D^{22}$ +15°, which was identified as (+)-selinane (IX) by a comparison of its infrared spectrum with that appeared in the literature.[5]

Deuterium Exchange Experiment of Tetrahydrodictyopterone (VIII).—Deuterium exchange was effected by heating VIII (32 mg.) in N sodium deuteroxide solution (0.5 ml.) and dry dioxane (1.5 ml.) at 100°C for 10 min. After cooling, the solvent was distilled off under diminished pressure. To the product was added a mixture of heavy water (0.7 ml.) and dry dioxane (1.5 ml.), and the mixture was heated and most of the solvent was then evaporated in vacuo. This procedure was repeated two times, and finally the residue was extracted with dry ether. Removal of the ether yielded tetrahydrodictyopterone-d_2 (24 mg.) as a colorless oil. Mass spectrum: *m/e* (rel. abund.) 224 (100), 222 (92), 178 (98), 163 (81), 135 (72), 109 (65), 81(64), 43(62).

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5) J. Pliva, M. Herac, V. Herout and F. Šorm, "Die Terpene. Sammlung der Spektren und Physikalischen Konstanten," Teil I. Akademie-Verlag, Berlin (1960).