Novel Eudesmane-Type Sesquiterpenes from *Alpinia japonica* (THUNB.) MIQ.

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Three novel eudesmane-type sesquiterpenes, 10-epi-5β-hydroperoxy-β-eudesmol (I), 10-epi-5α-hydroperoxy-β-eudesmol (II) and 4,10-epi-5β-hydroxydihydroeudesmol (III), have been isolated from the rhizomes of *Alpinia japonica*. Their structures were determined by spectroscopic methods and chemical conversions.

Keywords—*Alpinia japonica*; Zingiberaceae; sesquiterpene; eudesmane; peroxide; solvent shift; biosynthesis

In our previous studies on the chemical constituents of *Alpinia japonica*, the presence of eudesmanes, agarofurans, eremophilanes, guaianes and seco-guaianes has been reported.1,2) Our further work on the constituents of *A. japonica* has resulted in the isolation of three novel eudesmanes, 10-epi-5β-hydroperoxy-β-eudesmol (I), 10-epi-5α-hydroperoxy-β-eudesmol (II) and 4,10-epi-5β-hydroxydihydroeudesmol (III). In this paper, the determination of their structures is reported. The structural relationships between them and a possible biogenetic pathway of these compounds are also discussed.

![Chart 1](image)

Compounds I and II, whose spectral data were very similar to each other as mentioned below, were each obtained as colorless needles. Both of them have the same molecular formula, C_{15}H_{26}O_{3}, and the infrared (IR) spectrum shows absorptions of a prominent hydroxyl band at 3610 cm\(^{-1}\) and exomethylene at 3090 and 900 cm\(^{-1}\). However, no carbonyl absorption was indicated. The proton nuclear magnetic resonance (\(^1\)H-NMR) spectrum not only supported the presence of the exomethylene group (I: δ 4.79 and 5.03, each 1H, s; II: δ 4.91 and 5.10, each 1H, s) but also indicated the presence of a hydroxy isopropyl group (I: δ 1.32 and 1.35; II: δ 1.20 and 1.24), which was also supported by the fragment ion at \(m/z\) 59 in the mass spectrum (MS). The carbon 13 nuclear magnetic resonance (\(^13\)C-NMR) spectrum also showed the presence of two carbons bearing an oxygen function (I: δ 74.1 (s) and 87.0 (s); II: δ 72.9 (s) and 89.5 (s)) and indicated the absence of a carbonyl group. Since I and II showed a purple spot due to peroxide\(^3\) on a silica gel thin layer plate when treated with N,N-dimethyl p-phenylenediamine dihydrochloride, the remaining two oxygen atoms were assigned to the hydroperoxy group. Based on the above spectral data and biogenetic considerations, I and II were deduced to be an isomeric pair of 10-epi-5-hydroperoxy-β-eudesmol, probably biosyn-
thesized from 10-epi-γ-eudesmol by the "ene"-type reaction of a singlet oxygen with an olefin.4)

The dye-sensitized photooxygenation of 10-epi-γ-eudesmol with oxygen gave a mixture of the two isomeric hydroperoxides, I as the main product, and II as the minor product. The configurations of the hydroperoxide at C-5 were assigned on the basis of the pyridine-solvent shift5) of the reduction products (IV and V) in the 1H-NMR spectra (Table I) and the observation of internal hydrogen bonding in IV. Reduction of I and II with triphenylphosphine afforded IV and V, respectively. In the 1H-NMR spectra (pyridine-d₅), both methyl groups at C-11 of IV and V showed a downfield shift (ca. −0.2 ppm) because of the geminal deshielding effect. However, although the methyl group at C-10 of V showed a downfield shift of −0.30 ppm due to the vicinal deshielding effect, that of IV showed a downfield shift of only −0.04 ppm. Therefore the configurations of the hydroxyl group at C-5 in V and IV were determined to be α and β, respectively. The above assignment was supported by the presence of internal hydrogen bonding in a highly diluted solution of IV, but not V, as judged from the IR spectra.

The photooxygenation of 10-epi-γ-eudesmol gave compound I, the more stable isomer having a β-hydroperoxy group, as the main product, and compound II, the more unstable one having an α-hydroperoxy group, as the minor product. However, the fresh rhizome of A. japonica was found to contain II in a larger quantity than I.

Compound III was obtained as colorless needles (mp 130.0—132.0 ºC), having the molecular formula C₁₅H₂₈O₂, based on high-resolution MS. The presence of a hydroxy isopropyl group was indicated by the 1H-NMR (δ 1.25 ppm), IR (3620 cm⁻¹) and MS (m/z 59) spectra. Further the NMR spectrum showed the presence of two additional methyl groups (δ 1.10 and 1.04 ppm) and two hydroxyl groups (δ 3.76 ppm, disappeared on addition of D₂O). The catalytic hydrogenation of IV gave III. Therefore, the structure of III was determined except for the configuration of the methyl group at C-4. Since a pyridine-solvent shift of

![Chart 2](image)

| Table I. Pyridine-Solvent Shift (δCDCl₃−δPyridine-d₅) in 1H-NMR of III, IV and V |
|-----------------|-------|-------|
| III             | IV    | V     |
| Methyl group at C-4 | −0.06 |       |
| Methyl group at C-10 | −0.05 | −0.04 | −0.30 |
| Isopropyl methyl group at C-11 | −0.18 | −0.20ᵃ | −0.16ᵃ |

ᵃ The average shift value of isopropyl methyl groups at C-11.
\(-0.06\) ppm for the methyl group at C-4 of III was observed, as shown in Table I, the configuration of the methyl group at C-4 was established to be \(z\). Furthermore, this structure was supported by the pyridine-solvent shift of the methyl group at C-10 and the observation of internal hydrogen bonding in a highly diluted solution of \(\text{CCl}_4\).

From the biogenetic point of view, I, II and III are considered to be biosynthesized from 10-epi-\(\alpha\)-eudesmol, which is a possible precursor of agarofuran-type sesquiterpenes obtained from \textit{Alpinia japonica}, as discussed in our previous report.2

**Experimental**

All melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. Spectral data were obtained on the following instruments; optical rotation on a JASCO DIP-4, IR on a JASCO A-302, NMR on a Brucker AM400, MS on a Hitachi M-80. High-performance liquid chromatography (HPLC) was carried out on a C18 column system (Kusano Scientific Co., Tokyo) with IATROBEADS (60 \(\mu\) silica gel, IATRON CO., Tokyo) as the stationary phase.

**Extraction and Isolation** — The fresh rhizomes (70.0 kg) of \textit{Alpinia japonica} were extracted twice with methanol under an argon atmosphere. The methanol extract was partitioned with n-hexane, and the n-hexane layer was concentrated to give a yellow oil (65.0 g). The n-hexane extract was subjected to column chromatography on silica gel with an n-hexane-ethyl acetate gradient system. Repeated HPLC and \(\text{AgNO}_3\)-HPLC of each fraction using a benzene-ethyl acetate system, a benzene-chloroform-acetonitrile system, an n-hexane-ethyl acetate system and an n-hexane-chloroform-acetonitrile system gave I (100 mg), II (500 mg) and III (200 mg). Compounds I—III were recrystallized from n-hexane.

**Compound I (10-epi-\(\sigma\)-Hydroperoxy-\(\alpha\)-eudesmol):** Colorless needles, mp 131.0—133.0 \(^\circ\)C, \([\alpha]_D\) = -52.0 \(^\circ\) (c = 0.20, \(\text{CHCl}_3\)). MS \(m/z\)%: 254 (M\(^+\), 12, Caled for \(\text{C}_{13}\text{H}_{20}\text{O}_2\), 254.1879; Found 254.1875), 252 (9), 244 (10), 236 (10), 183 (20), 149 (80), 126 (100), 109 (52), 107 (57), 105 (57), 95 (100), 81 (55), 69 (42), 59 (71), 57 (100), 47 (27). IR (\(\text{CCl}_4\)) cm\(^{-1}\): 3610, 3400, 2940, 2880, 1650, 1460, 1400, 1385, 1380, 1260, 1145, 1100, 1060, 1020, 930, 900. \(^1\)H-NMR (\(\text{CDCl}_3\)) \(\delta\) ppm: 3.96 (3H, s), 1.32 (3H, s), 0.91 (3H, s), 4.78 (1H, dd, \(J=1.4, 1.4\) Hz), 4.82 (1H, dd, \(J=1.6, 1.6\) Hz).

**Compound II (10-epi-\(\sigma\)-Hydroxy-\(\alpha\)-eudesmol):** Colorless needles, mp 146.0—147.0 \(^\circ\)C, \([\alpha]_D\) = -48.6 \(^\circ\) (c = 0.21, \(\text{CHCl}_3\)). MS \(m/z\)%: 254 (M\(^+\), 5, Caled for \(\text{C}_{13}\text{H}_{20}\text{O}_2\), 254.1879; Found 254.1875), 252 (9), 244 (10), 236 (10), 183 (20), 149 (80), 126 (100), 109 (52), 107 (57), 105 (57), 95 (100), 81 (55), 69 (42), 59 (71), 57 (100), 47 (27). IR (\(\text{CCl}_4\)) cm\(^{-1}\): 3610, 3400, 2940, 2870, 1640, 1465, 1445, 1380, 1325, 1185, 1130, 900. \(^1\)H-NMR (\(\text{CDCl}_3\)) \(\delta\) ppm: 3.96 (3H, s), 1.20 (3H, s), 1.42 (3H, s), 0.91 (3H, s), 5.10 (1H, s). \(^1\)C-NMR (\(\text{CDCl}_3\)) \(\delta\) ppm: 72.9 (s), 87.0 (s), 111.1 (t), 148.7 (s).

**Compound III (10-epi-\(\sigma\)-Hydroxynaphtho-\(\alpha\)-eudesmol):** Colorless needles, mp 130.0—132.0 \(^\circ\)C, \([\alpha]_D\) = -21.8 \(^\circ\) (c = 0.12, \(\text{CHCl}_3\)). MS \(m/z\)%: 240 (M\(^+\), 5, Caled for \(\text{C}_{13}\text{H}_{20}\text{O}_3\), 240.2078; Found 240.2077), 238 (7), 230 (12), 203 (10), 182 (57), 161 (21), 147 (25), 135 (30), 123 (55), 121 (42), 109 (60), 95 (100), 81 (55), 69 (42), 59 (71), 57 (100), 47 (27). IR (\(\text{CCl}_4\)) cm\(^{-1}\): 3610, 3400, 2940, 2870, 1640, 1465, 1445, 1380, 1325, 1185, 1130, 900. \(^1\)H-NMR (\(\text{CDCl}_3\)) \(\delta\) ppm: 3.54 (3H, s), 1.25 (6H, s), 0.91 (3H, s), 4.78 (1H, dd, \(J=1.4, 1.4\) Hz), 4.82 (1H, dd, \(J=1.6, 1.6\) Hz).

**Hydrogenation of IV to Give I and II** — A 30 mm quartz tube enclosed by a 100 W mercury lamp was charged with a solution of 90 mg of 10-epi-\(\sigma\)-eudesmol and 20 mg of hematoporphyrin in 40 ml of methanol under ice-cold water. Oxygen was admitted through a gas dispersion tube and the mixture was irradiated for 20 min. Removal of the solvent under reduced pressure afforded a crude hydroperoxide, which was immediately subjected to HPLC (n-hexane : ethyl acetate = 3 : 2) to give I (20 mg) and II (4 mg).

**Reduction of I with Triphenylphosphine to Give IV** — An ether solution (2 ml) of I (15 mg) was treated with triphenylphosphine (25 mg) for a few minutes at room temperature, and then evaporated. The residue was subjected to HPLC (n-hexane : ethyl acetate = 7 : 3) to give colorless needles, IV (11 mg). MS \(m/z\)%: 238 (M\(^+\), 3), 220 (20), 205 (25), 162 (25), 147 (40), 124 (53), 95 (54), 58 (100). IR (\(\text{CCl}_4\)) cm\(^{-1}\): 3620, 3480, 3080, 2950, 2880, 1640, 1450, 1370, 1120, 1060, 970, 900. \(^1\)H-NMR (\(\text{CDCl}_3\)) \(\delta\) ppm: 0.86 (3H, s), 1.18 (3H, s), 1.19 (3H, s), 4.79 (1H, brs), 4.97 (1H, brs).
evaporated. The residue was subjected to AgNO₃–HPLC (n-hexane:ethyl acetate = 7:3) to give III as colorless needles (3 mg).

References