# Photooxygenation of 1,3-Cholestadiene and Related Compounds[1]

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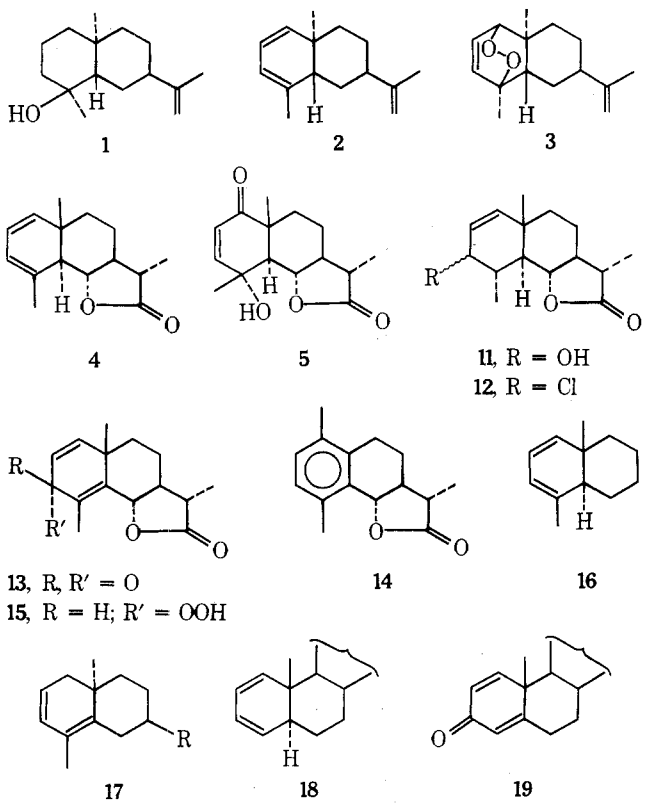
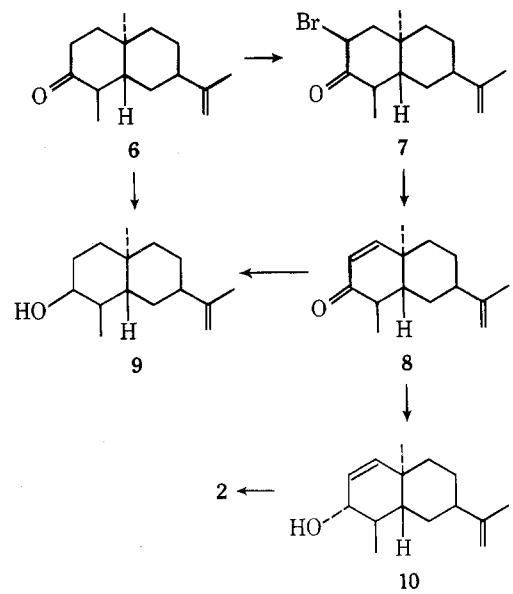
In an effort to effect stereoselective and regioselective total syntheses of the sesquiterpenes intermedeol (1) and tauresmisin (5), homoannular dienes (2) (5-epi-10-epieudesma-1,3,11-triene) and 4 (6, 11$\beta H$-eudesma-1,3-dien-6,13-olide) were subjected to photochemical oxygenation. Diene 2 gave a complex mixture of products, while 4 gave mixtures of santonin and hyposantonin, the result of a photochemical ene reaction. The expected endoperoxides could not be detected. 1,3-Cholestadiene (18) was also subjected to photochemical oxygenation and gave 1,4-cholestadien-3-one (19) as the only isolable product derived from 18. These results are discussed in terms of the steric requirements for endoperoxide formation. The syntheses of compounds 2 and 4 are described, and methods of preparation of 1,3-cholestadiene are discussed.

In the course of a general synthetic program in the sesquiterpene field, a variet of approaches to the 10-epieudesmane group of these natural products have been explored.[2] A major goal of this program was a convenient total synthesis of intermedeol[3] (5-epi-10-epieudesma-11-en-4$\beta$-ol, 1), a presumed biosynthetic precursor of the valencene–nookatone group of sesquiterpenes. An attractive regioselective and stereoselective synthetic approach to 1 involved the photooxygenation of 5-epi-10-epieudesma-1,3,11-triene (2), to give endoperoxide 3 which could be converted to intermedeol in a relatively few steps. In addition, the photooxygenation product of the related diene (4) derived from santonin[4] could serve as a precursor for another sesquiterpene, tauremisin (5).[5]




Triene 2 was prepared from 4-epi-5-epi-10-epieudesm-11-en-3-one (6)[6] as outlined in Scheme I. Utilizing a modification of a procedure employed in a total synthesis of occidentalol,[7] ketone 6 was condensed with ethyl formate and the resulting formyl compound brominated to give $\alpha$-bromo ketone 7, which was smoothly dehydrohalogenated to enone 8. Reduction of 8 with potassium tri-*sec*-butylborohydride[8] quite unexpectedly gave 4-epi-5-epi-10-epieudesm-11-en-3$\beta$-ol (9), the result of conjugate reduction, as the only isolable product.[9] The structure and stereochemistry of 9 were confirmed by its preparation from ketone 6 by reduction with potassium tri-*sec*-butylborohydride. In contrast, lithium aluminum hydride reduction of enone 8 gave a crystalline alcohol which, on the basis of its spectral properties (see Experimental Section), was assigned structure 10 in which the hydroxyl group is quasi-equatorial. Attempted dehydration of 10 by means of toluenesulfonic acid at room temperature[7] gave complex mixtures, while von Rudloff's procedure[10] afforded recovered alcohol. The dehydration of 10 was finally accomplished by use of the procedure utilized by a Syntex group for preparation of steroidal 1,3-dienes.[11] Reaction of alcohol 10 with thionyl chloride gave an unstable allylic chloride which on heating in dimethylformamide–pyridine afforded triene 2. Photooxygenation of 2, followed by treatment with basic alumina to convert the endoperoxide to the corresponding hydroxy enone,[12] gave a mixture of at least seven compounds, which on the basis of spectral data contained little if any of the desired product. In view of simultaneous experiments with diene 4 (see below) this reaction was not investigated further.

Scheme I




Base treatment of the endoperoxide derived from diene 4 would be expected to lead to a convenient synthesis of tauremisin (5), a sesquiterpene isolated simultaneously some years ago by two groups.[5] Although one total synthesis of this compound has been reported,[13] the final stages of the synthesis were carried out without the isolation or purification of intermediates and in very poor overall yield. Diene 4 has

been prepared by Corey in five steps from santonin and used in the synthesis of dihydrocostunolide.[4] In this synthesis of **4** the mixture of epimeric precursor alcohols (**11**) was dehydrated directly; however, in this work compound **4** was prepared from the mixture of epimeric allylic chlorides in the same manner used for the preparation of triene **1**. Photooxygenation of **4**, followed by treatment with basic alumina, gave no trace of tauremisin (**5**), but afforded instead mixtures of santonin (**13**) and hyposantonin (**14**). These products undoubtedly both arise from hydroperoxide **15**, santonin by the normal mode of decomposition of hydroperoxides, and hyposantonin by a variation of the dienol–benzene rearrangement. Hydroperoxide **15** is in turn derived from **4** by way of a photochemical ene reaction.[14] Although the photochemical ene reaction of singlet oxygen with homoannular dienes has been observed as a competing reaction with endoperoxide formation in a few cases,[14] at the time this work was completed the only other apparent example of the exclusive occurrence of the ene reaction of a cisoid conjugated diene was in the case of a highly hindered triterpene derivative.[15] The failure of the normal 1,4-cycloaddition reaction of singlet oxygen in that case was attributed to "steric hindrance". Following the completion of this work, however, Sasson and Labovitz reported that photooxygenation of diene **16** afforded only products from a photochemical ene reaction, while a similar diene lacking the angular methyl group reacted normally, giving the endoperoxide as a major product.[16] These authors attribute the failure of diene **16** to form an endoperoxide to "a strong 1,3-diaxial interaction between the angular methyl group and an ethylenic bridge". This explanation cannot, however, be correct, because the diaxial interactions in the endoperoxides derived from dienes **16**, **4**, and **2** are no worse than those in the endoperoxides derived from 2,4-cholestadiene[17] or two dienes (**17**, R = isopropyl[18] or isopropenyl[19]) closely related to **2** and **16**, which readily form endoperoxides.

In order to gain additional insight into the steric affects in the reactions of homoannular dienes, 1,3-cholestadiene (**18**)[20] was subjected to photooxygenation. When diene **18** which had been prepared from 3$\beta$-chlorocholest-1-ene by heating in dimethylformamide[11,20c] was subjected to photooxygenation, two crystalline compounds were obtained. The major product was 1,4-cholestadien-3-one (**19**), the result of the ene reaction, while the minor product (ca. 10%) was identified as the endoperoxide derived from 2,4-cholestadiene.[17] Since there is no reasonable mechanism for the formation of this endoperoxide from diene **18**, this product was assumed to be an artifact derived from 2.4-cholestadiene present as a contaminant in diene **18**. To confirm this conclusion, 1,3-cholestadiene was also prepared from the tosylhydrazone of 1-cholesten-3-one.[20b] Photooxygenation of **18** prepared in this manner gave a product which contained no endoperoxide, but which did contain a small amount of 2-cholestene, which was undoubtedly an impurity in the starting diene. The 2,4-cholestadiene present in the 1,3-diene prepared by Dauben's method probably arises from the pyridine hydrochloride catalyzed isomerization of **18** (see Experimental Section). The 2-cholestene present in **18** prepared by Herz's method may originate from some 3-cholestanone present in the 1-cholesten-3-one precursor of **18**, or it may arise during the reaction of the tosylhydrazone with methyllithium.

It is quite apparent that the photooxygenation of dienes structurally similar to 1,3-cholestadiene leads exclusively, or nearly exclusively, to products arising from photochemical ene reactions. This can be explained neither in terms of diaxial interactions (see above) nor in terms of "steric hindrance", since 1,3-cholestadiene is a relatively unhindered diene. Examination of Dreiding models of the endoperoxides derived from 1,3-cholestadiene and 2,4-cholestadiene indicates that there is considerable strain inflicted in the endoperoxide derived from the 1,3-diene as a result of fusing a second ring in a trans relationship to a full boat 2-cyclohexene system. Although there is also appreciable strain of the same type present in the endoperoxide derived from the 2,4-diene, qualitatively the strain appears to be less. Since a diene similar to **16** without the angular methyl group gives a endoperoxide in reasonable yield,[16] it is apparent that diaxial interactions must also play a role in determining the course of these reactions.[21]

## Experimental Section[22]

**2$\beta$-Bromo-4-epi-5-epi-10-epieudesm-11-en-3-one (7).** A solution of 6.45 g of 4-epi-5-epi-10-epieudesm-11-ene-3-one (**6**)[6] in 100 ml of dry ether was added slowly to a cold (ice bath), stirred mixture of 4.50 g of sodium hydride (50% dispersion), 50 ml of ethyl formate, 8 drops of methanol, and 200 ml of dry ether. The reaction mixture was then allowed to warm to room temperature and stirred for 18 h under nitrogen. Sufficient water was added to decompose the excess hydride and the reaction mixture extracted with three portions of iced 10% aqueous sodium hydroxide. The combined aqueous extracts were washed with ether, acidified with cold dilute hydrochloric acid, and extracted with ether. The ethereal extracts were washed with water and dried and the solvent removed at reduced pressure to give 5.83 g of formyl compound as a brown oil which was brominated without further purification.

To a stirred solution of 6.23 g of the above formyl compound in 150 ml of ethanol containing 30 g of barium hydroxide was added slowly 8.05 g of pyridimium bromide perbromide in 150 ml of ethanol. The reaction mixture was stirred at room temperature for 0.75 h, poured into water, and extracted with three portions of ether. The extracts were combined, washed with water, and dried and the solvent removed to give a yellow oil which slowly crystallized. Recrystallization from hexane gave 6.09 g (69%) of material, mp 53–63 °C, which was sufficiently pure for subsequent reactions. The analytical sample, mp 77–78 °C, was prepared by repeated recrystallizations from hexane: ir 5.76 $\mu$; NMR $\delta$ 1.10 (d, $J$ = 7 Hz, $CH_3CH$), 1.20 (s, 3 H, $CH_3$), 1.69 (s, 3 H, $CH_3C$=), 4.75 (m, 2 H, $CH_2$=C).

Anal. Calcd for $C_{15}H_{23}BrO$: C, 60.20; H, 7.75; Br, 26.71. Found: C, 60.23; H, 7.90; Br, 27.02.

**4-Epi-5-epi-10-epieudesma-1,11-dien-3-one (8).** To a solution of 5.76 g of bromo ketone **7** in 200 ml of dry dimethylformamide was added 6.0 g of lithium bromide and 8.0 g of lithium carbonate. The mixture was heated, with stirring, at 125 °C under nitrogen for 18 h, cooled, and poured cautiously into dilute aqueous acetic acid and the resulting suspension extracted with three portions of ether. The ethereal extracts were combined, washed well with water, and dried and the solvent removed to give a pale yellow oil. Distillation (150–170 °C, bath temperature, 0.04 mm) gave 3.44 g (83%) of ketone **8** as a colorless liquid: ir 5.99, 6.01 $\mu$; NMR $\delta$ 1.08 (s, 3 H, $CH_3$), 1.09 (d, 3 H, $CH_3CH$), 1.65 (d, $J$ = 1 Hz, $CH_3C$=), 4.69 (m, 2 H, $CH_2$=C), 5.48 (1 H d, $J$ = 9 Hz, CH=CHC=O), 6.25 (d, 1 H, $J$ = 9 Hz, CH=CHC=O).

For analysis the compound was converted to the 2,4-dinitrophenylhydrazone, mp 129–131 °C, from ethanol–ethyl acetate.

Anal. Calcd for $C_{21}H_{26}N_4O_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 63.20; H, 6.45; N, 14.01.

**4-Epi-5-epi-10-epieudesm-11-en-3$\beta$-ol (9). A.** A solution of 0.714 g of 4-epi-5-epi-10-epieudesma-1,11-dien-3-one (**8**) in 20 ml of dry tetrahydrofuran was added to 60 ml of a cooled (0 °C) 0.5 M solution of K-Selectride in tetrahydrofuran. The reaction mixture was stirred under nitrogen at 0 °C for 2 h and the excess hydride destroyed by the cautious addition of water. To the stirred reaction mixture was then added 50 ml of 2 N sodium hydroxide, followed by the cautious addition of 35 ml of 30% hydrogen peroxide. The reaction mixture was stirred at ambient temperature for 18 h, and the aqueous layer separated and washed with two portions of ether. The ethereal washings were combined with the original orgainc layer, washed with water and brine, and dried and the solvent removed at reduced pressure to give 0.504 (70%) of alcohol as a colorless oil. This material was identical with that prepared in part B below.

**B.** Reduction of 0.183 g of 4-epi-5-epi-10-epieudesm-11-en-3-one (**6**) using 20 ml of K-Selectride following the procedure described in part A gave 0.145 g (79%) of alcohol **9** as a colorless oil. Distillation (bp

140–150 °C, bath, 0.12 mm) gave the analytical sample as a viscous, water-white liquid: ir 2.91, 6.13, 11.33 μ; NMR δ 0.88 (s, 3 H, $CH_3$), 0.88 (d, 3 H, $J$ = 6 Hz, $CH_3CH$), 1.71 (s, 3 H, $CH_3C$=), 3.78 (m, 1 H, CHOH), 4.82 (m, 2 H, $CH_2$=).

Anal. calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.70. Found: C, 81.14; H, 11.65.

**4-Epi-5-epi-10-epieudesma-1,11-dien-3β-ol (10).** To a cooled (0 °C) solution of 2.76 g of unsaturated ketone **8** in 200 ml of dry ether was added 1.00 g of lithium aluminim hydride. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. Crushed ice was added cautiously to decompose the excess hydride and the ethereal solution decanted from the precipitated solids. The inorganic salts were washed with ether, the ethereal solutions combined and dried, and the solvent removed to give 2.48 g (90%) of oil which crystallized on standing. This material was essentially homogeneous to TLC and was used without purification for subsequent transformation. For analysis a small quantity of the alcohol was recrystallized from methanol-water to give white needles: mp 87–88 °C; ir 3.02, 6.18, 11.30 μ; NMR δ 0.99 (s, 3 H, $CH_3$), 0.99 (d, $J$ = 5 Hz, 3 H, $CH_3CH$), 1.72 (s, 3 H, $CH_3C$=C), 3.77 (br d, $J$ = 8 Hz, 1 H, CHOH), 4.88 (m, 2 H, $C_3H_2$=C), 5.45 (s, 2 H, CH=CH).

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.86, H, 11.00.

**5-Epi-10-epieudesma-1,3,11-triene (2).** To a cooled (0 °C) solution of 0.280 g of allylic alcohol **10** in 25 ml of dry benzene was added, with stirring, 1 ml of thionyl chloride. The reaction mixture was stirred at 0 °C for 0.5 h, allowed to warm to ambient temperature, and stirred for an additional 1 h. The solvent was removed at reduced pressure with gentle warming, and the residue taken up in ether. The ethereal solution was washed with 5% aqueous sodium carbonate and water and dried and the solvent removed to give the 3-chloro compound as an unstable, pale yellow oil. This material was taken up in 20 ml of dimethylformamide, 1 ml of pyridine was added, and the mixture was heated at reflux under nitrogen for 18 h. After cooling, the reaction mixture was poured into water and extracted with three portions of hexane. The hexane extracts were washed with successive portions of water, iced 5% hydrochloric acid, 5% sodium carbonate, and water and dried and the solvent removed at reduced pressure to give a yellow oil. This oil was taken up in hexane and chromatographed on 10 g of Merck alumina. Elution with hexane gave 0.170 g (53%) of hydrocarbon **2** as a colorless liquid which slowly decomposed on standing: ir 6.10, 11.21 μ; NMR δ 0.82 (s, 3 H, $CH_3$), 1.78 (br s, 6 H, $CH_3C$=), 4.85 (br s, 2 H, $CH_2$=), 5.60 (m, 3 H, CH=CHCH=C–); uv max ($CH_3OH$) 267 nm (ε 3600); mass spectrum $m/e$ (rel intensity) 202 (100), 187 (58), 159 (100), 157 54), 145 (92).

**6,11β*H*-Eudesma-1,3-dien-6,13-olide (4).** Allylic alcohol **11** was converted to diene **4** by the method described above for the preparation of 5-epi-10-epieudesma-1,3,11-triene. From 0.50 g of alcohol there was obtained, after recrystallization from hexane, 0.21 g (46%) of material, mp 83–86 °C (lit. mp 95–97 °C[4]). The spectral properties were in agreement with those reported by Corey, and the material was homogeneous to TLC (silica gel G, hexane–benzene, 1:1).

**Photooxygenation of 6,11β*H*-Eudesma-1,3-dien-6,13-olide.** A solution of 0.340 g of **4** in 170 ml of 95% ethanol containing 0.025 g of eosin and 1.5 ml of pyridine was irradiated at 0 °C with a 275-W Westinghouse sun lamp for 18 h while oxygen was bubbled through the solution. The solvents were removed at reduced pressure, and the residue was taken up in benzene–ether (1:1) and absorbed on 8 g of Merck alumina. After standing for 3 h, the column was eluted with benzene–ether (1:1) to give 0.154 g of semisolid which TLC (silica gel G, benzene–ethyl acetate, 6:1) showed was a mixture of five compounds, two of which accounted for the bulk of the material. The $R_f$ value of the principal component of this mixture corresponded to that of santonin, while the $R_f$ value of the other major component corresponded to that of hyposantonin. Trituration of the crude mixture with ether afforded 0.063 g of santonin (**13**), mp and mmp 169–171 °C. In another run, 0.138 g of crude material was dissolved in benzene and chromatographed on 10 g of Woelm silica gel. The first benzene–ethyl acetate (5:1) fractions gave 0.021 g of hyposantonin (**14**), which was identical with a sample prepared earlier,[23] while the final fractions eluted with the same solvents gave 0.026 g of santonin. The intermediate fractions afforded 0.021 g of mixtures of santonin, hyposantonin, and two minor constituents of the reaction mixture.

**1,3-Cholestadiene (18).** This compound was prepared either by the method of Dauben[20b] or that of Herz.[20c] Using Dauben's procedure, 9.96 g of crude 1-cholesten-3β-ol gave 2.74 g (29%) of diene: mp 59–60 °C; $[\alpha]^{21}D$ +84° (*c* 0.57) (lit. mp 60–61 °C, $[\alpha]^{23}D$ +78° [20b]). Neither the yield nor quality of the product could be improved by purification of alcohol or the intermediate allylic chloride. From 2.00 g of the tosylhydrazone of 1-cholesten-3-one, mp 166–168 °C dec (lit. mp 168–170 °C dec[20c]), using Herz's procedure there was obtained 0.390 g of diene, mp 55–58 °C, $[\alpha]^{20}D$ +66° (*c* 0.96) (lit. mp 67–68 °C, $[\alpha]^{20}D$ + 73° [20c]), plus a quantity of unreacted hydrazone. The spectral properties of material obtained by both methods were in agreement with those reported by Dauben.[20c]

When a sample of 0.121 g of diene **18** was heated at reflux in 25 ml of dimethylformamide for 24 h, it was recovered unchanged; however, the addition of 1 ml of pyridine and 3 drops of concentrated hydrochloric acid (conditions which duplicate Dauben's dehydrohalogenation) gave a gummy mixture of hydrocarbons. 1,3-Cholestadiene as originally prepared by Tamm and Albrecht[20a] was reported to have mp 67–68 °C, $[\alpha]D$ +73°.

**Photooxygenation of 1,3-Cholestadiene.** Diene **18** prepared by Dauben's method was photooxygenated in the manner described above for photooxygenation of **4**. From 1.160 g of diene in 200 ml of 1:1 benzene–ethanol containing 4 ml of pyridine and 0.030 g of eosin, there was obtained, after treatment with basic alumina, 1.107 g of crude material which was dissolved in hexane–benzene (4:1) and chromatographed on 100 g of Merck alumina. Elution with hexane–benzene (3:1) gave 0.103 g of the endoperoxide derived from 2,4-cholestadiene, mp 107–109 °C, which was identical with a sample prepared by photooxygenation of the diene.[17] Elution with hexane–benzene (1:1) gave 0.528 g of 1,4-cholestadien-3-one (**19**), mp and mmp 108–111 °C. The spectral properties were identical with those of a sample prepared by an alternate route. Elution with benzene gave 0.049 g of a mixture containing dienone **19** and small quantities of two other unidentified compounds.

Photooxygenation of 0.311 g of diene **18** prepared by Herz's procedure gave 0.083 g of dienone **19** and 0.063 g of 2-cholestene as needles from acetone, mp 67–69 °C. This material has an infrared spectrum identical with that of a sample, mp 67–68 °C, prepared by the method of Mauthner,[24] mmp 67–69°C.

**Registry No.**—**2**, 60184-24-9; **4**, 4678-04-0; **6**, 28290-27-9; **7**, 60184-25-0; **8**, 60184-26-1; 8 2,4-DNPH, 60184-27-2; **9**, 60209-18-9; **10**, 60184-28-3; **11**, 4678-03-9; **18**, 4117-49-1.

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(21) It should be noted that in the reaction of diene **16** lacking the angular methyl group, approximately 10% of the product arises from the ene reaction as it does with dienes **17** (ref 17 and 18). The differences in energy of activation for the ene reaction and endoperoxide formation are apparently rather small, and a slight increase in the energy of activation for the endoperoxide reaction in dienes structurally similar to 1,3-cholestadiene apparently decreases its rate relative to that of the ene reaction to the point where the ene reaction predominates.
(22) Melting points were determined on a Kofler hot stage apparatus and are

uncorrected. Infrared spectra were taken as liquid films on sodium chloride plates or as KBr disks using a Perkin-Elmer Model 137 spectrophotometer and are reported in microns. Nuclear magnetic resonance spectra were obtained using a Perkin-Elmer Hitachi R-24 spectrometer with deuteriochloroform as solvent. All spectra are reported in parts per million relative to tetramethylsilane ($\delta$). Mass spectra were determined using a Du Pont 21-490 mass spectrometer at 70 eV ionization potential. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

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# Isolation and Structural Elucidation of New Potent Antileukemic Diterpenoid Esters from *Gnidia* Species[1,2]

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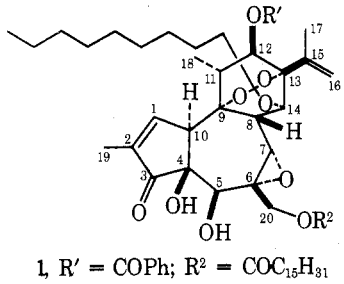
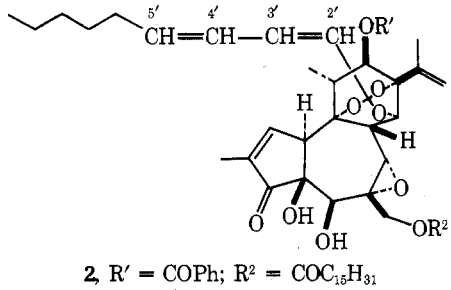
The isolation and structural elucidation of the new potent antileukemic principles, gnidilatin 20-palmitate (1), gnidilatidin 20-palmitate (2), and gnidilatin (3), and the new toxic diterpenoids, gnidilatidin (4) and gnidiglaucin (5), are reported. Esters 1 and 2 were proven to be C-20 palmitate esters of gnidilatin (3) and gnidilatidin (4), respectively, by acylation of 3 and 4 with palmitoyl chloride. Methanolysis of 1, 3, and 5 afforded the tetrol 6 as a common parent diterpenoid ortho ester. The tetrol 7 was obtained from 2 and 4. Catalytic hydrogenation of 3 and 4 gave dihydrognidilatin (8).

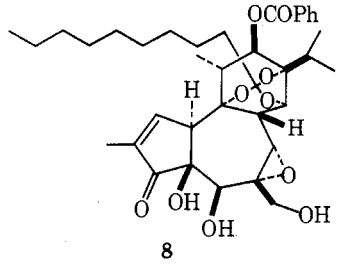
In the course of a continuing search for tumor inhibitors from plant sources, we found that alcoholic extracts of *Gnidia latifolia* Gilg.[3] and *Gnidia glaucus* Fres.[4] (Thymelaeaceae) showed significant activity in vivo against P-388 leukemia in mice.[5] We report herein the isolation and structural elucidation of the potent antileukemic principles, gnidilatin 20-palmitate (1), gnidilatidin 20-palmitate (2), and gnidilatin (3), and the companion toxic principles gnidilatidin (4) and gnidiglaucin (5).



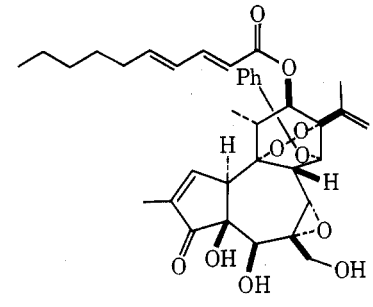
1, R′ = COPh; R² = $COC_{15}H_{31}$
3, R′ = COPh; R² = H
5, R′ = $COCH_3$; R² = H
6, R′ = H; R² = H



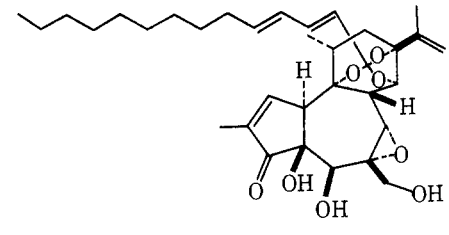
2, R′ = COPh; R² = $COC_{15}H_{31}$
4, R′ = COPh; R² = H
7, R′ = H; R² = H



8



9



10

Fractionation of the ethanol extract of *G. latifolia*, guided by a combination of an in vivo assay for antileukemic activity (P-388) and a goldfish toxicity test,[6] revealed that both the antileukemic and piscicidal activity were concentrated in the chloroform layer of a chloroform–water partition. Column chromatography on SilicAR yielded two active fractions (A and B) upon elution with ethyl acetate–benzene (1:9 and 3:7, respectively). Column chromatography of fraction A on silica gel and subsequent preparative layer chromatography on silica gel gave two closely related compounds, gnidilatin 20-palmitate (1), $C_{53}H_{78}O_{11}$, and gnidilatidin 20-palmitate (2), $C_{53}H_{74}O_{11}$. Successive column chromatography of fraction B on silica gel, then Celite, followed by preparative TLC on silica gel gave two closely related compounds, gnidilatin (3), $C_{37}H_{48}O_{10}$, and gnidilatidin (4), $C_{37}H_{44}O_{10}$.

The initial spectral data (ir, NMR) of these compounds indicated that they were structurally related to gnididin (9)[7] and huratoxin (10),[8] previously isolated from *Gnidia lamprantha* Gilg. (Thymelaeaceae) and *Hura crepitans* L. (Euphorbiaceae), respectively. The NMR spectrum of gnidilatidin (4) was almost identical with that of gnididin (9) except for the signals for the diene vinyl protons (at C-2′, 3′, 4′, and 5′),