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<td>Fujita, Eiichi; Fuji, Kaoru; Nagao, Yoshimitsu; Node, Manabu; Ochiai, Masahito</td>
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Kyoto University
The Chemistry on Diterpenoids in 1975 Part-I

Eiichi Fujita, Kaoru Fuji, Yoshimitsu Nagao, Manabu Node, and Masahito Ochiai*

Received May 6, 1976

I. INTRODUCTION

This is one of a series of our annual reviews1-11) on diterpenoids chemistry. The classification of the compounds is the same as that adopted in our reviews since 1969. This review covers the literature published between January and June 1975.

II. PODOCARPANE DERIVATIVES

Unusual partial inversion of configuration at two remote centers on demethylation

Formulae (1)-(8)

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of (+)-12-methoxypodocarpa-8, 11, 13-triene (1) was reported. Thus, treatment of optically pure 1 with HI/HBr/AcOH and a trace of H₃PO₄ gives, as a major product, a non-racemic mixture of (+)-podocarpa-8, 11, 13-trien-12-ol (2) and its enantiomer 3. Ozonolysis of 2 and subsequent transformations afforded the lactone 4, a tobacco flavoring agent, and the bicyclic acetate 5, a compound with a woody odor. The compounds 6 and 7 were obtained by the boron trifluoride induced rearrangement of 8.

Chromium trioxide oxidation of trimethoxypodocarpatriene (9) gave a quinone 11, whereas under similar conditions 10 gave a diketone 12.

Methyl and ethyl esters of sterically hindered diterpenoic acids were easily hydrolyzed into the parent carboxylic acids by the action of acetic or chloroacetic acid in quinoline or DMF. A new method of geminal alkylation via α-trimethylene-dithiocyclobutanones was reported. The synthesis of 13 in Chart I demonstrates the synthetic utility of the new method.

Cyclization of the epoxide 14 gave the podocarpane derivatives 15 and 16 along with 17.

(Chart I)

<table>
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<tr>
<th>Formulae (9)-(12)</th>
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<tbody>
<tr>
<td>(9) R = αH</td>
</tr>
<tr>
<td>(10) R = βH</td>
</tr>
<tr>
<td>(11)</td>
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<td>(12)</td>
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(Chart 1)

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<th>Formulae (14)-(17)</th>
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<tr>
<td>(14)</td>
</tr>
<tr>
<td>(15) R' = OMe, R'' = H</td>
</tr>
<tr>
<td>(16) R' = H, R'' = OMe</td>
</tr>
<tr>
<td>(17)</td>
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(198)
The Chemistry on Diterpenoids in 1975. Part I

Detailed discussion on the dehydration reactions in the mass spectra of podocarpan-12- and -14-ols has been presented.19)

III. LABDANE DERIVATIVES

Manoyloxyde (18) along with other diterpenes was isolated from the cypress essential oil.20) Sagittaria sagittifolia was proven to contain a new diterpene, sagittariol (19).21) The structures of four isomeric diterpenes (20) isolated from Green tobacco were determined by spectroscopic means and conversion into 12-norambreinolide (21).22)

A new diterpene, hedychenone (22) was isolated from Hedychium spicatum.23) The growth inhibitor for silkworm larvae from Avocado leaves was identified as dimethyl sciadinonate (23).24) The structure of lagochilin (24) was determined by an X-ray analysis.25)

The reaction of labd-8(17)-en-13-ol (25) with thallium (III) nitrate in methanol gave rise to the isolation of 26, 27, 28, and 29. The reaction mechanism is briefly discussed.26) Transesterification of sclareol (30) with triethyloorthoacetate and subsequent rearrangement gave (E)- and (Z)-ethyl 8-hydroxylabd-13-en-15-ylacetate 31
and 32. Cyclization of these esters with tin (IV) chloride in benzene was also described.27)

\[
\text{Formulae (25)-(32)}
\]

A simple method of degradation of the readily available labdane group of diterpenes to drimanic sesquiterpenes was reported.28) The illustrative example is the conversion of (+)-ambreinolide (33) into (+)-drimane-8, 11-diol (34) by the reaction with D. D. Q. followed by ozonolysis and reduction. The structures of the products obtained by NaBH₄ or LiAlH₄ reduction of 35 were discussed.29)

\[
\text{Formulae (33)-(35)}
\]

A total carbon shift analysis of several representatives of the labdane family using ¹³C-NMR spectroscopy was presented.30, 31) The effect of sclareol (30) on the germination and growth of rust fungi in vitro was described.32)

Several labdane derivatives are cited in the following three review articles. Their titles are “Chemicals from Trees”33) “Neutrals in Southern Pine Tall Oil”34) and “Halogenated Organic Compounds from Marine Plants.”35)

IV. CLERODANE DERIVATIVES

The first diterpene possessing a cis-clerodane skeleton, linaridial (36) was isolated...
The Chemistry on Diterpenoids in 1975. Part I

Clerodane

from *Linaria japonica*.\(^{36}\) An X-ray analysis of a key diterpene 37 from *Solidago arguta*, published at nearly the same time, served another example of *cis*-clerodane-type diterpene.\(^{37}\)

\[ \text{Formulae (36)-(37)} \]

V. PIMARANE AND ISOPIMARANE DERIVATIVES

Pimarane and Isopimarane

Sandaracopimara-8(14), 15-diene (38) and isopimaric acid (39) were isolated from the cypress essential oil\(^{20}\) and *Podocarpus lambertius*,\(^{28}\) respectively. The structure of iso-virescenol B (40), an aglycon of glycoside in the culture media of the fungus *Acremonium luzulae*, was determined by an X-ray analysis.\(^{39}\)

\[ \text{Formulae (38)-(40)} \]
A new diterpene 41 was isolated from *Osteospermum subulatum*. Lagascol (42) and the known lagascatriol (43) along with other type of diterpenes were isolated from *Sideritis serrata*.41)

![Formulae (41)–(47)]

Functionalization of 10-methyl group in isopimar-8β-ol (44) was accomplished by the hypoiodite oxidation and by the photorearrangement of its nitrite 45.42)

Biosynthetic origin of the substituents at C-4 of virescenols A (46) and B (47) was determined by 13C-NMR spectroscopy.43)

Structure and physiological properties of momilactones A (48) and B (49), growth regulating substances in rice husk, were reviewed in Japanese.44)

![Formulae (48)–(49)]

Autoxidation of isopimaric acid gave acidic products, which were characterized.45)

Pimaranes and isopimanes are also cited in the foregoing reviews.33, 34)

VI. ABIETANE DERIVATIVES

Dehydroabietane (50) has been isolated from the cypress essential oil (*Cuprusus sempervirens*).20) From leaves of *Podocarpus lambertius*, 8-abieten-15-ol (51) was iso-
lated. Inuroyleanol (52) and 7-keto-royleanone (53) have been isolated from the roots of Inula royleana and their structures established. Some diterpenoids related to abietic acid (54) as common resin acids of pine were described in a review on chemicals from trees. In a review on neutrals in southern pine tall oil, abietane type diterpenoids were also described.

Five new spiro-abietane diterpenes, coleone M (55), N (56), P (57), Q (58), and R (59), were isolated from Plectranthus caninus. Coleon O (60) was found in similar glands of Coleus somaliensis.

A review containing abietane type diterpenoid pigments was published. Synthetic transformations of dehydroabietic acid derivative 61 shown in Chart 2 were reported. Furthermore, compound 62 was also obtained in 25% yield by reduction of the corresponding nitro compound and in 40% yield by amination of the corresponding bromo compound.
Applications of oxidative and non-oxidative photorearrangements of nitrosoamides were illustrated. Namely, N-nitroso-N-acetyldehydroabietylamine (63) rearranged to give stable 6α-nitroso (64) and 6α-nitrate (65) derivatives respectively.

Unexpected rearrangements of photolevopimaric acid derivatives were published. Thus, treatment of 66 with Lewis acids resulted in rearrangement to 67. Jones oxidation of 68 proceeded with rearrangement to bicyclo [2.1.1.] hexanone 69. Treatment of 70 with tosyl chloride resulted in rearrangement to 71. An unusual oxidation of 68 to the lactones 72 and 73 with Fétizon's reagent was observed. Solvolytic reactions of tosylate 74 resulted in rearrangement to 75 and 76. The compounds 66 and 68 were prepared from 78, derived from methyl levopimarate (77) by irradiation, by epoxidation and hydroboration-oxidation, respectively.

rac-Dehydroroyleanone (81) was synthesized from 3-oxo-trimethoxy-podocar-
The total synthesis of \textit{rac}-royleanone (82) was achieved.\textsuperscript{53} The sequence is shown in Chart 3.

\textbf{VII. TOTARANE DERIVATIVES}

In a review on diterpenoid pigments, modified totarane type compounds were described.\textsuperscript{43} From bark of \textit{Podocarpus lambertius}, 3\textbeta\textendash hydroxytotarol (83), 4\textbeta\textendash carboxynortotarol (84), macrophylllic acid (85) were isolated.\textsuperscript{83}
The structure of podolide (86), a new antileukemic norditerpene dilactone from *Podocarpus gracilior*, was established by the X-ray analysis. The absolute configuration was assigned on the basis of the observation of a negative Cotton effect in the CD spectrum.54)

The structure of inumakilactone (87) was solved by a single crystal X-ray analysis.55) It was confirmed that the structure of the bisnorditerpenoid molecule was different from that previously proposed56) in respect of the orientation of the epoxy group on ring A.

The molecular structure of nagilactone A diacetate derived from X-ray analysis,57) as shown in (88), was shown to be consistent with that previously proposed58) on the basis of the chemical and spectroscopic data.

Antitumor activity of nagilactones, B (89), C (90), D (91), and E (92), and a related lactone (93) was evaluated.59)

**VIII. CASSANE DERIVATIVES**

Cassane

Formulae (94)–(97)
Isolation of unstable alkaloids from *Erythrophleum chlorostachys* was reported. Among them, structures of cytotoxic alkaloids, norerythrostachaldine (94) and its naturally occurring $3\beta$-acetate (95), were established.

Preparation of lactone (96) from diol (97) with silver carbonate on Celite was published.

**IX. Kaurane Derivatives**

From leaves of *Podocarpus lambertius*, phyllocladene (98), isophyllocladene (99), and 17-isophyllocladenol (100) were isolated.

*ent*-6α, 7α, 17-Trihydroxy-16αH-kauran-19-oic acid (101) and *ent*-6α, 7α, 16β, 17-tetrahydroxykauran-19-oic acid (102) were identified by GC–MS from the endosperm of *Echinocystis macrocarpa*. (See also Section XI.) In the essential oil of *Araucaris araucana*, ent-kaurene was shown to be contained together with other diterpenoids.

From *Sideritis theezans*, siderol (103), isolinearol (104), isosidol (105), sideridiol (106), sideroxol (107), a new diterpene shown to be epoxy-isolinearol (108), and isofoliol (109) were identified.
The structure of 110 for mascaroside, a bitter glycoside from Coffea vianneyi, was elucidated by spectral data and X-ray analysis.

Microbial oxidation of 17-norkauran-16-one (111) by the fungus Rhizopus nigricans produced a dihydroxy compound (112) and the structure was established by X-ray analysis of the acetate derivative. It was reported that incubation of 111 and 113 with Aspergillus niger gave C-3 equatorial alcohols 114 and 115, respectively, whereas compound 116 gave 3β-alcohol 117 and 3-ketone 118 which was identical with corresponding compound derived from calliterpenone.

Two new antibacterial metabolites, phlebiakauranol (119) and phlebianorkauranol (120) were isolated from Phlebia strigosozonala and shown to have highly oxygenated kaurane structures by X-ray analysis.

16, 17-Dihydroxy-9(11)-kauran-18-oic acid (121) was isolated from roasted coffee beans (Coffea arabica) and synthesized from compound 122. Several experiments for stevioside productivity of Stevia rebaudiana were reported. Enzymic hydrolysis of stevioside (123) to steviol (124) was undertaken using crude hesperidinase.

16-Bromodihydroenmein diacetate (125) was dehydrobrominated with lithium.
chloride in DMF to give a product, the structure of which was elucidated as the intermolecular ether (126).70

\[ R' = \text{glucose}, \quad R'' = \text{glucose} \]

Formulae (123)-(126)

The formolysis of tosylate 127 followed by basic hydrolysis gave mixtures which contained atisane type products [128, 129, and 130] of 1, 3-hydride shift.75)

\[ OTs \]

Formulae (127)-(130)

Rearrangement of the phenylsulfonylhydrazone of ent-beyeran-16-one (131) with sodium methoxide in \([2H]\) methanol yielded ent-[13, 14\(\alpha\)-\(2H\)]16-methoxykaurane (132), ent-[13, 14\(\alpha\)-\(2H\)]kaur-16-ene (133), and ent-[13, 14\(\alpha\)-\(2H\)]kaur-15-ene (134) together with ent-[16-\(2H\)]beyer-15-ene (135). Bridgehead enolization of ent-17-nor[13, 14\(\alpha\)-\(2H\)]kauran-16-one (136) was demonstrated by oxidation of the ketone, before and after heating with potassium t-butoxide, to the lactones 137 and 138, respectively.76) (See also section X.)

\[ R' = R'' = \text{H} \]

Formulae (131)-(141)

A novel rearrangement of the mesylate 139, derived from lucidusculine (140)
into olefine 141 was described.\textsuperscript{77}

A short synthesis of optically active $d$-isophyllocladene (99) and $d$-phyllocladene (98) was published.\textsuperscript{78} Namely, rearrangement of the ketone 142 leads to $d$-isophyllocladene-14-one (143), which can be converted into 99 or 98, as shown in Chart 4.

\begin{center}
\begin{tikzpicture}
\node (142) at (0,0) {\includegraphics[width=1.5in]{chart4}};
\node (143) at (1.5,0) {\includegraphics[width=1.5in]{chart4}};
\node (98) at (3,0) {\includegraphics[width=1.5in]{chart4}};
\end{tikzpicture}
\end{center}

The stereoselective synthesis of $d$-phyllocladene (98) from $l$-abietic acid (54) was reported.\textsuperscript{79} The sequence is shown in Chart 5.

\begin{center}
\begin{tikzpicture}
\node (54) at (0,0) {\includegraphics[width=1.5in]{chart5}};
\node (98) at (1.5,0) {\includegraphics[width=1.5in]{chart5}};
\end{tikzpicture}
\end{center}

In a communication on an improved method for methoxymethylation, preparation of compounds 144, 145, and 146 was described.\textsuperscript{80}

\begin{center}
\begin{tikzpicture}
\node (144) at (0,0) {\includegraphics[width=1.5in]{chart5}};
\node (145) at (1.5,0) {\includegraphics[width=1.5in]{chart5}};
\node (146) at (3,0) {\includegraphics[width=1.5in]{chart5}};
\end{tikzpicture}
\end{center}

From incubation of [17-$^{13}$C]-labeled dienol 147 in Gibberella fujikuroi, three acidic ent-kauranoid metabolites were isolated as their methyl esters [148, 149, and 150].\textsuperscript{81}
Metabolism of \( \text{ent-}[17\text{C}]\)kaurenol (151) and \( \text{ent-}[17\text{C}]\)kaurenal (152) by germinating *Hordeum distichon* was investigated and the initial steps of the biosynthetic pathway to gibberellins, that is, \( \text{ent-kaurenol} \), \( \text{ent-kaurenal} \), \( \text{ent-kaurenoic acid} \) (153), to \( \text{ent-7\alpha-hydroxy kaurenoic acid} \) were proved.\(^{82}\) Metabolic pathways from \( \text{ent-kaurenoic acid} \) (153)\(^{97}\) and \( \text{ent-15\alpha-hydroxy-kaurenoic acid} \) (154)\(^{87}\) to the fungal gibberellins were investigated. (See Section XI.) In the ring B contraction step in gibberellin biosynthesis, \( \text{ent-7\alpha-hydroxy-kaurenoic acid} \) (155) was discussed.\(^{101}\) (See Section XI.)

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**Formulae (147)–(155)**

---

**X. Beyerane Derivatives**

\( \text{d-Hibaene} \) (156) was found in the essential oil of *Araucaria araucana*.\(^{84}\) Two

---

**Formulae (156)–(160)**

(211)
new beyerane type diterpenes, tabarral (157) and benuel (158), were isolated from *Sideritis serrata*. The previously reported diterpenes, jativatriol (159) and conchitriol (160), were also obtained from the same source.\(^{41}\)

Rearrangement of the phenylsulfonylhydrazone of ent-beyeran-16-one (131) was reported. In the paper, the NMR spectra of ketones 131 and 161 were discussed in detail.\(^{76}\)

Correlation of the diterpenoids jativatriol (159) and sideritol (209) was published.\(^{83}\)

The *Sideritis* diterpene SP–2 was identified as 162 by the chemical conversion of 162 into *ent*-beyerane.\(^{84}\)

**XI. GIBBERELLANE DERIVATIVES**

The following gibberellin constituents of the endosperm of *Echinocystis macrocarpa* were identified by GC–MS. They are GA\(_4\) (163), GA\(_7\) (164), iso-GA\(_7\) (165), GA\(_{24}\) (166), and GA\(_{20}\) (167).
(166), GA25(167), two isomers of GA13(168), and GA40(169), respectively. The structure of a new gibberellin, GA43, was established by partial synthesis.63)

The structure of a new gibberellin (A90) isolated from the culture filtrate of Gibberella fujikuroi was determined as 170 on the basis of 13C NMR measurements and conversion into deoxygibberellin A5 methyl ester (171).85)

The structure and stereochemistry of a 1-hydroxy-3-oxo-gibberellin derivative was established to be 172 by X-ray analysis.86)

A new gibberellin (A45) (173) was obtained from seeds of Pyrus communis. Its biosynthesis from a kaurene precursor was also investigated.87) (See Section IX.) The 13C NMR spectra of a series of gibberellins were measured and analyzed almost completely. The spectrum of 13C-enriched gibberellins (mixture of A1 and A3) produced by Gibberella fujikuroi fed with sodium [1-13C] acetate was also reported.88)

The gas chromatography of gibberellins and gibberellin-O-glucosides treated with silylating reagents was reported.89) Mass spectra of several gibberellins were detected.90)

The partial synthesis of gibberellin A37(174) from gibberellin A13(168) was published. Selective reduction of the least reactive carboxy-group (C10-COOH) in gibberellin A13 was successively achieved through formation of the 20, 3-lactone 175, which gave the 3α-hydroxy-epimer 176 of gibberellin A37. This epimer was converted into gibberellin A37(174) via Meerwein-Ponndorf reduction of 177. The sequence is illustrated in Chart 6.91) Meerwein-Ponndorf reduction of the 3-oxo-gibberellins 177, 178, and 179 gave 50% or greater yields of the 3β-epimers, whereas the 3-oxo-20, 19-lactone 180 afforded the 3α-hydroxy-epimer predominantly.91)
Dilactone 181 was irradiated with a Hg high pressure lamp for 82 hr under argon at 25–30° to give 50% yield of lactone 182 by the intramolecular photoaromatization.\(^9^2\)

\[
\begin{align*}
(178) & & \quad (179) & & \quad (180) & & \quad (181) & & \quad (182) \\
\end{align*}
\]

Formulae (178)–(182)

\(p\)-Bromophenacyl ester 183 of gibberellic acid was treated with a large excess of the fluoroamine in methylene chloride at room temperature to yield two isomeric difluoro-esters which were identified as 184 and 185 by their spectroscopic properties. De-esterification of the esters 184 and 185 with Zn dust in glacial acetic acid at room temperature gave the corresponding difluorogibberellins 186 and 187.\(^9^3\)

\[
\begin{align*}
(183) & \quad R^1 = R^3 = OH, \quad R^2 = CH_2CO\left(\bigodot\right)Br \\
(184) & \quad R^1 = R^3 = F, \quad R^2 = CH_2CO\left(\bigodot\right)Br \\
(185) & \quad R^1 = R^3 = F, \quad R^2 = F \\
(186) & \quad R^1 = R^3 = F, \quad R^2 = H \\
(187) & \quad R^1 = H, \quad R^2 = F \\
\end{align*}
\]

Formulae (183)–(187)

The partial synthesis of 6\(\beta\)-methyl-7-nor-gibberellin-A\(_3\) (189) from compound 188 was performed. The outline is shown in Chart 7.\(^9^4\)

\[
\begin{align*}
(188) & \quad (189) \\
\end{align*}
\]

Chart 7

Photochemical cycloaddition of ethylene to 3-dehydro-gibberellin A\(_3\) (190) yielded a mixture of adducts 191 and 192 in a ratio of 3 : 1.\(^9^5\)

\[
\begin{align*}
(190) & & \quad (191) & & \quad (192) \\
\end{align*}
\]

Formulae (190)–(192)

The biosynthetic relationship of the gibberellins in Gibberella fujikuroi was reported. A comparison of the results of feeding gibberellin A\(_{12}\) alcohol 193 and gibberellin A\(_{12}\) (214)
The Chemistry of Diterpenoids in 1975. Part I

(194), in terms of the distribution of mevalonate, to *G. fujikuroi*, revealed that there was a divergence between the pathways leading to the 3-hydroxylated and the non-3-hydroxylated gibberellins at the C-7 aldehyde stage. The distribution of label between the C19 and C20 gibberellins after 6 and 24 hours incubations suggested that the free C20 gibberellins [A14 (195), A36 (196), and A12 (168) or A15 (197), A24 (166), and A25 (167)] might not lie on the direct pathway to the C19 gibberellins. Gibberellins A4 (163) and A7 (164) were transformed into gibberellic acid (198). Incubation of gibberellin A12 (194) with *G. fujiduroi* might be used to prepare gibberellins A24 (166) and A35 (167).

Metabolic pathways from *ent*-kaurenoic acid to the fungal gibberellins were investigated using mutant B1-41a of *Gibberella fujikuroi*. The metabolism of substrates normally produced by wild-type strains of *G. fujikuroi* was determined in resuspended cultures of the mutant B1-41a at pH 3.5 and 7.0. The metabolites were identified by GC-MS and GC-Radiocounting. From the results at pH 3.5 the metabolic steps from *ent*-kaurenoic acid to the fungal gibberellins were deduced. The oxidation level at which C-20 is lost in the formation of C19-gibberellins could not be determined. *ent*-7-Oxokaurenoic acid did not serve as a precursor of gibberellin A12 aldehyde (199). At pH 7.0 the pathway from gibberellin A12 (194) was diverted completely to 3-deoxygibberellins such as gibberellin A9 (200).

The effect of gibberellins on growth of pea seedling internode was reported. Elongation of internode segments of dwarf pea seedling exercised 4 mm below the plumular hook was stimulated by GA3 (198) but not by GA1 (201) or GA5 (202).
However, all three gibberellins induced cell elongation in the region from which this segment was isolated on application to intact seedlings.\(^{98}\)

An enzyme from *Phaseolus vulgaris* seeds which hydroxylates GA\(_{1}\) (201) to GA\(_{8}\) (203) was characterized. This hydroxylase was specific for GA\(_{1}\) and did not hydroxylate either pseudo-GA\(_{1}\)-[\(^{3}\)H] (204) or rearranged 16-keto-GA\(_{1}\)-[\(^{3}\)H] (205).\(^{99}\)

Tritium-labeled gibberellins [GA\(_{1}\) (201), GA\(_{4}\) (163), GA\(_{5}\) (202), GA\(_{8}\) (203) and GA\(_{20}\) (206)] were fed to immature bean seeds 18 days after anthesis and their metabolic pathways were investigated.\(^{100}\)

The mechanism of ring contraction (155\(\rightarrow\)199) and 6α-hydroxylation (155\(\rightarrow\)207) using the endosperm preparation of *Cucurbita maxima* seed and the \(^{3}\)H: \(^{14}\)C double labeled substrate of 155 was studied. It was demonstrated that the formation of GA\(_{12}\)-aldehyde (199) and ent-6α, 7α-dihydroxykaurenoic acid (207) involves the loss of one hydrogen atom from the 6-position in ent-7α-hydroxykaurenoic acid (155).\(^{101}\)

**XII. ATISANE DERIVATIVES**

The essential oil of *Araucaria araucana* included ent-atisirene (128) and ent-isoatisirene (129).\(^{84}\)

From *Sideritis serrata*, two atisane type diterpenes were isolated with some other type
diterpenes. They were serradiol (208) and sideritol (209). The former was new.\textsuperscript{41}

Treatment of methyl \textit{ent}-trachyloban-19-oate (210) with thallic oxide in acetic acid afforded many products. The paper on formation of the major products had been published.\textsuperscript{102} Now, the structures of seven minor products, 211–217, and the mechanism of the oxidative cleavage were reported.\textsuperscript{103}

\[ \text{Chart 8} \]

The room temperature formolysis of the tosylates, 218 and 219, followed by basic hydrolysis, gave mixtures which contained products [128, 129, and 130] of 1, 3-hydride shift.\textsuperscript{75} On formolysis of kaurane tosylate 127, the same result was obtained. (See Section IX.)

A convenient synthesis of trachylobane (221) \textit{via} a reductive homoallylic cyclization of compound 220 with LiAlH\textsubscript{4} was reported. (See Chart 8).\textsuperscript{104}

The diterpenoids sideritol (209) and jativatriol (159) were correlated by transformation of each into diketone 222.\textsuperscript{83}

A chemical conversion of atisine (223) into lycocotonine type compounds was published. The detail is described in Section XIII.
The structural relationships among various aconitine-type alkaloids were re-examined on the basis of the structure of delphisine (224).105)

The structure of iliensine (225), isolated from Delphinium biternatum, was determined by means of the spectroscopic methods.106)

The structure of acononine (226) isolated from Aconitum monticola was determined on the basis of spectroscopic and chemical evidence.107) Karacolidine was isolated from tubers of Aconitum karacolicum and its structure 227 was elucidated by NMR and mass spectroscopy and chemical transformations.108)

The chemical conversion of atisine (223) into the ketone 228 possessing a lycocotonine skeleton and the X-ray structure determination of the product were published. The outline of the conversion sequence is shown in Chart 9.109)
The structures of baccatin-III (229), -IV (230a), -VI (230b), -VII (231) and 1-dehydroxybaccatin-IV (232) were determined.\textsuperscript{110}

The geranylnerol derivative ligantrol (233) and its monoacetate (234) were iso-

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**XIV. TAXANE DERIVATIVES**

The geranylnerol derivative ligantrol (233) and its monoacetate (234) were iso-
lated from Liatris elegans and their structures established. The absolute stereochemistry assigned to C-11 and C-14 (11R, 14S) was deduced by degradation to a known lactone 235 of established absolute configuration.111)

\[
\begin{align*}
(233) & \quad R = \text{H} \\
(234) & \quad R = \text{Ac} \\
(235) & \\
(236) & \quad R = \text{O} \\
(237) & \quad R = \text{H, OH} \\
(238) & \\
(239) &
\end{align*}
\]

Formulae (233)–(239)

Four novel constituents of Nicotiana tabacum were identified as 236, 237, 238, and 239. Their possible formation from cembrene-type precursors was briefly discussed.112) (See Chart 10.)

\[
\begin{align*}
(236), (237), (238) \xrightarrow{a + c \quad (R = \text{H})} (239) \\
(236), (237), (238) \xrightarrow{d + c \quad (R = \text{OH})}
\end{align*}
\]

Chart 10

Sinulariolide, a novel diterpene lactone was isolated from Sinularia flexibilis. Its absolute structure was established by X-ray diffraction as depicted in 240.113) 6, 20-Epoxylathyrol (241) was isolated from Macaranga tanarius.114) From the seed oil of Euphorbia lathyris the known diterpenoids 241, ester L₁, and ester L₂ were isolated.115)

\[
\begin{align*}
(240) & \\
(241) &
\end{align*}
\]

Formulae (240)–(241)

Reaction of 241 with acids in THF led to simple fission of the epoxy ring and yielded the corresponding hydrid derivatives. When anhydrous methanol was used as the solvent, reaction of 241 with hydrochloric acid gave the novel macrocyclic trichloride 242 which has the jatrophane skeleton. Reaction with sulfuric acid afforded

\[
(220)
\]
The Chemistry on Diterpenoids in 1975. Part I

the transannular cyclization product 243 and methoxyhydrin 244.\textsuperscript{116)"

\[ \text{\textsuperscript{(C6H\textsubscript{5})CHz.000off.HH.}} \]

\[ \text{\textsuperscript{Aco}} \]

\[ \text{\textsuperscript{CACH\textsubscript{4}CO0H~AcCN3.CHcoo~\'oH \hspace{1cm} d~\hspace{1cm} orle}} \]

Formulae (242)–(244)

Reaction of 241 with barium methoxide afforded 245, whereas the reaction with sodium methoxide gave 246.\textsuperscript{117) The photochemical reactions of 241 and 246 were shown to afford 247 and 248, respectively.\textsuperscript{118)}

\[ \text{\textsuperscript{(z~z) (243)(244')}} \]

\[ \text{\textsuperscript{(245)(246)}} \]

\[ \text{\textsuperscript{(z47) R' = COCH \textsubscript{2} C\textsubscript{6}H\textsubscript{5},}} \]

\[ \text{\textsuperscript{R''= Ac}} \]

\[ \text{\textsuperscript{(aggg) ft' = Rz= 11}} \]

\[ \text{\textsuperscript{(247)}} \]

\[ \text{\textsuperscript{(248)}} \]

Formulae (245)–(248)

Two new toxic compounds, named kansuinine A and B were isolated from \textit{Euphorbia kansui}, and the structures were determined as 249 and 250, respectively.\textsuperscript{119,120,121)"

\[ \text{\textsuperscript{(z49)}} \]

\[ \text{\textsuperscript{(250)}} \]

Formulae (249)–(250)

The structure 251 of fusicoccin J, a minor glucoside produced by \textit{Fusicoccum amygdali}, was determined by its synthesis from fusicoccin (252).\textsuperscript{122) The carbon-13 NMR spectra of 252 and its derivatives were investigated.\textsuperscript{123) From \textit{Aleurites fordii} fruits, two new diterpenes were isolated. The structure 253 was assigned by its chemical transformation into 255. The structure of another toxic constituent was established as 254 by partial synthesis from 253.\textsuperscript{124)}

The structure 251 of fusicoccin J, a minor glucoside produced by \textit{Fusicoccum amygdali}, was determined by its synthesis from fusicoccin (252).\textsuperscript{122) The carbon-13 NMR spectra of 252 and its derivatives were investigated.\textsuperscript{123) From \textit{Aleurites fordii} fruits, two new diterpenes were isolated. The structure 253 was assigned by its chemical transformation into 255. The structure of another toxic constituent was established as 254 by partial synthesis from 253.\textsuperscript{124)"
From *Daphne mezereum* an antileukemic principle, mezerein (256) was isolated and characterized. The novel antileukemic diterpenes, gnididin, gniditrin and gnidicin were isolated from *Gnidia lamprantha*, and their structures were determined as 257, 258, and 259, respectively. New irritant compounds 260, 261, and 262 were isolated from *Hippomane maminella*. From *Euphorbia resinifera*, two yellow-orange staining, non-irritant compounds 263 and 264 as well as three blackish-brown staining irritant *Euphorbia* factors RL.20 (265), RL.9 (266) and RL.14 (267) were isolated. Similarly, compound 266 was isolated from *Euphorbia unispina*.

Autoxidation of phorbor ester 268 gave 269-274 characterized by T. L. C. and partial synthesis. A new diterpene triol 275 was isolated from *Eremophila decipiens*. Spectroscopic and degradative methods with 1, 2-^{13}C_{2}-acetate and 2-^{14}C-4R-
The Chemistry on Diterpenoids in 1975. Part I

\[ \text{(268)} \quad R = \text{CH}_2\text{OH} \]
\[ \text{(269)} \quad R = \text{CHO} \]

Formula (268)–(275)

\(^3\text{H}\)-mevalonate precursors showed that aphidicolin (276) arose from initial chair-boat cyclization of the diterpene chain followed by successive H-shift, cyclization and rearrangement steps, as shown in Chart 11.\(^{131}\)

The review on the biogenetic type synthesis and reaction of terpenoids was published.\(^{132}\)

The papers "Stereochemistry of diterpene alkaloids in acylation and alkaline hydrolysis",\(^{133}\) "Structure of vulgarol, a new diterpenoid from Marrubium vulgare"\(^{134}\) and "Structure of aconorine"\(^{135}\) were published. Cembrene, dehydroabietinal, palustral, epimanool, epitorulosol, larixol, larixol acetate, and isoprimarinol were isolated from oleoresins of Larix sibirica, L. sukaczewii, and L. czekanovskii.\(^{136}\)
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