<table>
<thead>
<tr>
<th>Title</th>
<th>The Chemistry of Diterpenoids in 1975. Part-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Fujita, Eiichi; Fuji, Kaoru; Nagao, Yoshimitsu; Node, Manabu; Ochiai, Masahito</td>
</tr>
<tr>
<td>Citation</td>
<td>Bulletin of the Institute for Chemical Research, Kyoto University (1977), 55(3): 323-354</td>
</tr>
<tr>
<td>Issue Date</td>
<td>1977-09-30</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/2433/76736">http://hdl.handle.net/2433/76736</a></td>
</tr>
<tr>
<td>Type</td>
<td>Departmental Bulletin Paper</td>
</tr>
<tr>
<td>Textversion</td>
<td>publisher</td>
</tr>
</tbody>
</table>

Kyoto University
The Chemistry on Diterpenoids in 1975. Part-II

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

Received May 30, 1977

I. INTRODUCTION

This is one of a series of our annual reviews1-12 on diterpenoids chemistry. The classification of the compounds is the same as that adopted in our reviews since 1969. This review covers the literatures published between July and December 1975 and also omissions in part-I.

II. PODOCARPANE DERIVATIVES

The benzylic acid rearrangement of the dioxo ester 1 derived from abietic acid gave a gibberellane derivative 2, whose stereochemistry was determined unequivocally.13

A method for angular functionalized methylaton via bromocyclopropane 4, which was obtained by the abnormal Reimer-Tiemann reaction of 3 with bromoform followed

* Fujita Eichi, Fuji Kaoru, Nagao Yoshimitsu, Node Manabu, and Ochiai Masahito: Laboratory of Physiological Activity, Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu 611, Japan.
E. Fujita, K. Fuji, Y. Nagao, M. Node, and M. Ochiai

by cyclization, was reported.\textsuperscript{14} The bromocyclopropane 4 has a high reactivity towards various nucleophiles to give the ring-opened products. Thus, variously functionalized methyl group can be introduced into the angular position by a choice of nucleophiles. (Chart 1)

![Chart 1](image)

Reactions of methyl dehydroabietate derivatives 5 and 6 with aluminum chloride were examined.\textsuperscript{15} Epimerization at C-10 and/or deisopropylation might depend on the hydroxy group on the aromatic ring. The results are summarized in Chart 2.

![Chart 2](image)

Selective cleavage of β-keto and vinylogous β-keto esters by 3-quinuclidinol was published.\textsuperscript{16} An application of the reaction to the podocarpane derivative 7 giving rise to 8 was noted.
The stereochemistry of the products (e.g. 9 and 10) from the photoaddition between podocarpane derivatives having $\alpha, \beta$-unsaturated ketone moiety and olefins was discussed by the relative stability of the excited state.\textsuperscript{17}

Carbon-13 nuclear magnetic resonance spectra of a series of ring C substituted podocarpane derivatives were reported.\textsuperscript{18}

### III. LABDANE DERIVATIVES

A new diterpenoid, vulgarol (11), was isolated from Marrubium vulgare.\textsuperscript{19} The major metabolite of Nicotiana glutinosa was identified as a mixture of 12 and 13, and the minor metabolite of this species was tentatively assigned the structures 14, 15, and 16. Their potential technological significance is also discussed.\textsuperscript{20} Three ent-labdane type diterpenes 17, 18, and 19 were isolated from Hymenea coubaril.\textsuperscript{21}

Agathic acid (20), agatholic acid (21) and imbricatolic acid (22) as well as abietane type diterpene, sugiol, were isolated from Araucaris angustifolia.\textsuperscript{22} A number of labdane oxides, 18-deoxylazarcardenasol (23) and 18-benzoxyllazarcardenasol (24) from Palafaxia rosea,\textsuperscript{23} gomeraldehyde (25), 13-epigomeraldehyde (26), gomeric acid (27) and 13-epigomeric acid (28) from Sideritis gomerae,\textsuperscript{24} and barbatol (29) from S. arborescens,\textsuperscript{25} were isolated and characterized. ent-Labd-13-ene-8$\alpha$, 15-diol was also isolated from S. gomerae.\textsuperscript{24}

(325)
Two diterpenes, 30 and 31, were isolated from *Pamburus missionis*. The crystal and molecular structures of two highly oxygenated labdane type diterpenes, lasiocoryin (32) and nepetaefolin (33), were determined by X-ray analyses.

Chemical conversion of manool (14) into anticopalic acid (34) has been reported. The outline is shown in Chart 3. Manool (14) was also converted into beyerane derivatives, which is described in section X.

A formal total synthesis of methyl 12S- and 12R-hydroxylabd-8(17)-en-19-oates, (35) and (36) respectively, isolated from *Juniperus phoenicea*, has been achieved. The labdane side chain was formed by the nucleophilic addition of s-butyllithium to
Chemistry on Diterpenoids in 1975. Part-II

the bicyclic acid 37 or the aldehyde 38, prepared from podocarpic acid.

Oxidation of sclareol (13) led to a complex mixture. The structure of each component was characterized. Acid catalyzed cyclization of methyl anticopalate (39) and methyl Z-anticopalate gave rise to 40 and its 14-epimer 41. Methyl isoanticopalate (40) was selectively attacked from the α-side on hydroboration, PtO₂—H₂ reduction, and OsO₄ oxidation, whereas no selectivity was recognized on its 14-epimer (41). Studies on carbon-13 NMR spectra of several labdane derivatives were published.

IV. CLERODANE DERIVATIVES

Diterpenoid 42 was isolated from Evodia floribunda. Columbin (43) and its C-8 epimer, isocolumbin were isolated from Dioscoreophyllum cumminsii.
V. PIMARANE AND ISOPIMARANE DERIVATIVES

The structure of hallol isolated from *Podocarpus hallii* was determined as 44. Isopimarane type diterpenes, 45 and 46, as well as kaurane derivatives were isolated from *Siegesbeckia pubescens*. *Sideritis reverchonii* was found to contain eight known diterpenoids including lagascol (47) and lagascatriol (48) together with a new diterpenoid belonging to beyerane type.

Reduction of 49 with Zn–AcOH, Li–NH₃, or Me₂CuLi gave 50, whereas 51 was obtained together with 50 by Ca–NH₃ reduction of 49. Epoxidation of methyl sandaracopimarate gave the α- and β-epoxides 52 in 1:1 ratio. The tetracyclopentadecene 53 was prepared by tosylation of 3-oxo-19-hydroxisopimaradiene (54) followed by cyclization with t-BuOK–t-BuOH.
In a review titled "Growth regulating substances of plant origin", a number of diterpenoids including pimarane type are described.\(^{45}\)

VI. ABIETANE DERIVATIVES

Sugiol (55) was isolated from Araucaria angustifolia\(^{22}\) and Libocedrus bidwillii.\(^{46}\)

Reactions of methyl dehydroabietate derivatives having electron-donating group at aromatic C-ring with aluminum chloride were examined.\(^{15}\) (See section II, Chart 2.) Reaction of 12-acetyl ester 56 with aluminum chloride gave predominant trans-isomer 57 accompanied by the cis-isomer 58. In the other case of reactions of methyl dehydroabietate derivatives having electron-withdrawing group, 7-oxo ester 59 did not react even under the drastic conditions. But 7-oxo ester having a hydroxyl or a methoxyl group at 12 or 14-position was deisopropylated to give only the respective trans-deisopropyl isomer.\(^{47}\)

Conversion of dehydroabietic acid (60) to a steroid skeleton was attempted. Synthesis of the 3-oxo compound 61 having a steroid type A ring was successfully completed from 62 or 63 derived from 60 via intermediates 64 and 65.\(^{48,49}\)
Compound 1 derived from abietic acid (66) was converted into compound 2.13) (See Section II.) A ring substitution of hydrofluorene compound derived from abietic acid (66) was accomplished.50) (See also Section XI.)

Kaurene and 13β-kaur-16-ene (phylocladene) were synthesized from abietic acid (66).51) (See Section IX.) The phenacylidene ester 67 underwent novel rearrangements on refluxing with an excess of aluminum chloride to afford 68 and 69 in 57 and 5% yields.52) (See Chart 4.)

The steroidal D-rings (70 and 71), along with 72 and 73, were synthesized by the use of a part or whole of the carbon units of the isopropyl group of abietic acid (66).53)

Total synthesis of rac-sugiol (55), rac-nimbiol (74), and rac-ferruginol (75) was achieved.54) The sequence is shown in Chart 5.
The azodehydroabietic acids, 76, 77, and 78, were prepared. Treatment of abietyl chloride with excess amines gave abietamides, which were reduced to abietylamines by LiAlH₄. Abietic acid (66) was oxidized by passing oxygen at 30–150°C.  

Antileukemic diterpenoid, triptolide (79) and tripdiolide (80) were cited in a short review article. (See also Section VII.)

VII. TOTARANE DERIVATIVES

The structure of podolide (81), an antileukemic norditerpene dilactone isolated from Podocarpus gracilior, was determined by an X-ray analysis.

A review on the growth regulating substances of plant origin, in which several totarane derivatives were cited, was published. (See also Sections V and XV.)  Also in the foregoing review, several totaranes were cited.
The structure of 3β-acetoxynorerythrosuamine (82), a highly cytotoxic alkaloid from *Erythrophleum chlorostachys*, was determined.\(^\text{60}\)
From *Cacalia bulbifera*, *ent*-16-kauren-19-ol (83), *ent*-16-kauren-19-al (84), *ent*-16-kauren-19-oic acid (85), and *ent*-kauran-16-ol (86) were isolated. Sideridiol (87), and foliol (88) were isolated from *Sideritis chamaedryfolia*, and siderol (89) from *S. hyssopifolia*, and foliol (88), sidol (90), and linearol (91) from *S. luteola*.

From *Coffea arabica* beans, *ent*-16-kauren-19-ol (83) was isolated. The compounds 92, 93, and 94 were isolated from *Siegesbeckia pubescens*, and 93 and 94 showed antiinflammatory activity. (See also Section V.) The structure and absolute configuration of calliterpenone was established as 3-oxo-13α-kaurane-16,17-diol (95). This conclusion confirmed the structure proposed by Ahmad and Zaman, and the formula suggested previously by Chatterjee *et al.* was revised.

From the leaves of *Pieris japonica* were isolated deacylpieristoxin-B, pieristoxin-C, asebotoxin-I (96), graayanotoxin-II (97), graynotoxin-III (98), and two new diterpenes, pieristoxin F and pieristoxin G, to which the structures 99 and 100 were presumed, respectively.

The mass spectra of carbon-13-labeled kaurene and some related compounds were investigated.

C−α and C−β, previously isolated from seed of *Phaseolus coccineus*, were shown...
respectively to be 101 and 102. \(^{(67)}\) (See also Section XI.) The synthesis of gibberellin \(A_{15}\) methyl ester and gibberellin \(A_{37}\) methyl ester from enmein (103), and their more direct total synthesis via the key intermediate 104 were published.\(^{(68)}\) (See also Section XI.)

The full details of the previous communication of the synthesis of 16-kaurene (105) and 13\(\beta\)-kaur-16-ene (106) from abietic acid (66) were published.\(^{(51)}\) (See also Section VI.) The formation of the allylic nitrates, 107 and 108, in the reactions of both ent-16-kaurene (109) and ent-15-kaurene (110) with thallium trinitrate (TTN), and a [3, 3]-sigmatropic rearrangement between 107 and 108, were published.\(^{(69)}\)

Benzilic acid-type rearrangement of lactone derived from compound 111 by treatment with oxygen in t-BuOK-t-BuOH gave a gibberellane derivative.\(^{(70)}\) (See also Section XI.) Incubation of 17-norkauran-16-one (112) and ent-17-norkauran-16-one (113) with Rhizopus nigricans gave mixtures of mono- and dihydroxy-derivatives (114–117 and 118–121, respectively).\(^{(71)}\)
Steviol (122) was rapidly metabolized by the mutant B1-41a of *Gibberella Fujikuroi*. The initial product, *ent*-7α-hydroxy derivative 123, was further metabolized to 124, 125, 126, and several gibberellins.\(^7\) (See also Section XI.)

In *Gibberella fujikuroi* cultures, *ent*-[^3β-3H, 17-14C]kaurene was converted to gibberellic acid with retention of the tritium label at the 3α-position. The evidence for the stereochemistry of 3-hydroxylation also permitted the stereochemistry of the 'proton-initiated' cyclization step in gibberellic acid biosynthesis to be deduced.\(^7\) (See Chart 6).

Thinichrograph analysis was established for simple quantitative analysis of stevioside (127) in *Stevia rebaudiana*,\(^7\) and for the same purpose, the optimal condition for the enzymic hydrolysis of 127 and quantitative analysis of the resulting steviol (122) by gas chromatography were studied.\(^7\)}
A new diterpenoid acetate was isolated from *Sideritis reverchonii* and its structure was estimated to be 12-acetyl jativaltriol (*ent*-12α-acetoxy-15-beyerene-1β, 17-diol) (128). Furthermore, eight known diterpenoids including beyerene type compounds, tobarrol (129), benanol (130), jativaltriol (131), and conchitriol (132), were also isolated.41) A communication about analysis of $^{13}$C NMR spectra of *ent*-beyerane (133), *ent*-7α, 12α, 17-triacetoxybeyerane (134), and *ent*-beyere derivatives, 135, 136, and 137 were published. A good agreement between experimental and calculated $^{13}$C chemical shifts for *ent*-beyere (133) was shown.76)

The solvolysis of the *ent*-methyl 12β-tolysulfonyloxybeyeron-19-oate (138) was published. Acetolysis gave only products resulting from a single Wagner-Meerwein shift [the *ent*-14(13→12)abeo-beyeranes, 139, 140, 141, and 142], whereas formolysis and trifluoroacetolysis gave products from further rearrangement in addition to the starting beyerane system [formates of *ent*-12-methyl-17-noratisanol (143) and *ent*-beyeranol (144); trifluoroacetates of 143, 144, and 145]. The rearrangements were discussed in terms of intermediate carbocation stabilities and lifetimes in the various solvents.77) The X-ray analysis of the *p*-bromobenzoate (146) derived from the product 139 of the solvolysis of 138 was undertaken.78)

* See also section IX, ref. 75.
Synthesis of beyerane type compounds through a photochemical cycloaddition of $\Delta^{14}$ podocarpen-13-one to ethylene or 1, 2-dichloroethylene was reported. The sequence is shown in Chart 7.

Besides polyoxygenated ent-kauranes, occurrence of Gibberellins A$_8$, A$_{17}$, A$_{20}$, and A$_{28}$ in Phaseolus coccineus seed was shown by GC–MS characterization of the hydrolysis products. Isolation of gibberellins A$_5$ and A$_{32}$, and gibberellin
A32 acetonide from *Prunus persica* was reported\(^{79}\) and the structures of gibberellin A32 and its acetonide were elucidated to be 147 and 148 respectively.\(^{80}\) The latter compound was concluded to be an artifact product from gibberellin A32 in the isolation process.\(^{80}\)

\[ \text{Diagram 147} \]
\[ \text{Diagram 148} \]

The \(^{13}\)C NMR spectra of some C19 gibberellins were assigned and the labeling pattern of gibberellin A3 from [2-\(^{13}\)C]mevalonic acid was confirmed.\(^{81}\) The mass spectra of trimethylsilyl ethers of six gibberellin-\(\beta\)-glucopyranosyl ethers and five gibberellin-\(\beta\)-D-glucopyranosyl esters were discussed. The fragmentation patterns were shown to be affected by the structural variations of the aglycones.\(^{82}\)

It was shown that the lactone ring of gibberellin A3 was destroyed by gamma-ray irradiation in dilute solution, whereas the basic gibberellane skeleton remained intact.\(^{83}\) Oxidation of gibberellin A3 by MnO\(_2\) gave lactone 149. 3-Dehydrogibberellin A3 (150) and its methyl ester were shown to be subject to Michael addition at C-1.\(^{84}\) Partial synthesis of gibberellin-A3-(7)-aldehyde (152) from 7-alcohol 151 was carried out by its oxidation with N-chlorosuccinimid-dimethylsulfoxide complex at \(-25^\circ\) to aldehyde followed by alkaline hydrolysis.\(^{85}\) The alcohol (151) was obtained together with carboxylic acid 153 by NaBH\(_4\) reduction of a dimeric anhydride 154 which was derived from 153 by dehydration with DCC.\(^{86}\)

\[ \text{Diagram 149} \]
\[ \text{Diagram 150} \]
\[ \text{Diagram 151} \]
\[ \text{Diagram 152} \]
\[ \text{Diagram 153} \]

3-Dehydrogibberellin A3 (150) upon n\(\rightarrow\)n\(^*\)-excitation of the enone chromophore was transformed in good yield to the corresponding ring A phenolic acid. The corresponding methyl ester under the same UV-irradiation conditions underwent inter-
molecular cycloaddition leading to two dimerization products. For explanation of this divergent crystal-controlled photoreactivity an X-ray analysis of 150 was performed, and the molecular packing determined.87)

As described in Section II, the stereochemistry of the hydroxy diacid 2, which was obtained by the benzylic acid rearrangement of the dioxo ester 1, was determined.13) Moreover, the rearranged compound 2 and its dimethyl ester were concluded to have a nonsteroidal form.13)

Several hydrofluorenes with A-ring substituent were synthesized from 1-abiatic acid.58)

The gibberellane derivative 155 was prepared starting from epicandicandiol using benzilic acid-type rearrangement as a key step.70) A synthesis of rac-compound 156 starting from methyl p-hydroxybenzoate was reported.88) The 2-carboethoxy-methyl-6-methoxy-indenone (157) was synthesized in good yield. Diels-Alder addition of 157 to 1, 3-butadiene afforded compound 158. The corresponding acid 159 was cyclized to 160, which on catalytic hydrogenation gave 161.88)

\[
\begin{align*}
\text{156} & \quad \text{157} & \quad \text{158} \\
\text{160} & \quad \text{161}
\end{align*}
\]

The synthesis from suitable indane derivatives of tetracyclic compounds 162 and 163, possible intermediates for the total synthesis of gibberellin A₄, was published.90)

\[
\begin{align*}
\text{162} & \quad \text{163}
\end{align*}
\]

The syntheses of gibberellin A₁₅ methyl ester (164) and gibberellin A₇ methyl ester (165) from enmein (103) and their total syntheses from the relay compound 10461) which has been derived from 5-methoxy-2-tetralone (166) were published.88) The sequence is shown in Chart 8.
The metabolism of gibberellins A₉ (170), A₂₀ (171), and A₂₉ (172) in immature seed of Pisum sativum CV. Progress No. 9 was investigated. The results of this experiment using tritiated gibberellins suggested that in vivo GA₉ (170) may not be the principal precursor of GA₂₀ (171) and that conversion of GA₂₀ to GA₂₉ is normal metabolic sequence. Furthermore, [³H]GA₂₀ (171) was injected into mature leaves of Bryophyllum daigremontianum under long- and short-day conditions. It was converted to GA₂₉ (172), 3-epi-GA₁ (173), C/D-ring-rearranged GA₂₀ (174), and two minor metabolites. 

\[ R^1 = R^2 = R^3 = H \]  
\[ R^1 = R^2 = H ; R^2 = OH \]  
\[ R^1 = R^3 = OH ; R^2 = H \]  
\[ R^1 = H ; R^2 = R^3 = OH \]
Chemistry on Diterpenoids in 1975. Part-II

Translocation and metabolism of [3H]gibberellins (A1, A4, A5, and A20) by light-grown Phaseolus coccineus seedlings were investigated.\(^94\)

Radioactive gibberellin A\(_3\) applied to seedlings of Pharbitis nil strain Violet was converted to one single metabolite which was tentatively identified as GA\(_3\)-glucoside.\(^95\)

The initial metabolism of steviol (122) to 13-hydroxylated ent-kauranes by mutant B1-41a of Gibberella fujikuroi was described in Section IX.\(^72\) Further metabolism produced GA\(_{12}\) (175), GA\(_1\) (176) as the major products and GA\(_{18}\) (177) as the minor product. From GA\(_{12}\) (175) were metabolized GA\(_{17}\) (178), GA\(_{29}\) (179), and GA\(_{30}\) (171).\(^72\)

Stereochemistry in the biosynthesis of gibberellin A\(_3\), (especially of cyclization and hydroxylation) was studied.\(^73\) (See Section IX.) Several biochemical reports on gibberellins and related compounds were published.\(^96-104\)

A review about utilization of gibberellin for modification of barley grain into malt without germination was published.\(^105\)

**XII. ATISANE DERIVATIVES**

From Sideritis reverchonii, two known atisane type diterpenes [serradiol (180) and sideritol (181)] were isolated.\(^41\)

Chemical and crystallographic data were presented for a new diterpenoid, ent-atis-13-en-7\(\alpha\), 16\(\alpha\), 17-triol (182), isolated from Sideritis angustifolia as a minor component together with the major diterpene sideritol (181).\(^106\)
A communication about chemical conversion of kobusine (183) involving cleavage of the bridged C-14, C-20 bond by a novel fragmentation reaction was published. The outline of the conversion sequence is shown in Chart 9.107

XIII. ACONANE DERIVATIVES

The structure of delectine (184), new diterpene alkaloid from Delphinium dictyocarpum, was determined by spectroscopy and chemical transformations into O, O-dimethyllycoctonine. The structure of iliensine (185) was determined by IR, NMR, and mass spectroscopy and chemical transformations into O-methylacomonine and nor-anhydroxyiliensine (186). The structure of aconorine (187), isolated
from *Aconitum orientale*, was determined by spectroscopy and chemical transformation into columbianine (188), isolated from *A. columbianum*.110)

A simple and stereospecific conversion of compound 189 to the aconite alkaloid model (delphinine-type) 190 was published. The outline of this synthetic route is shown in Chart 10.111)

![Chemical structures and synthesis scheme](image-url)

**Chart 10**

**XIV. TAXANE DERIVATIVES**

Taxicin-I (191) was cited in a review related to the method for preparation of bridgehead-olefins.112)
XV. THE OTHERS

The capacity of cell-free extracts of castor bean seedlings for synthesis of casbene (192) was compared for seedlings which had been germinated under sterile conditions and seedlings which were intentionally exposed to fungal cultures. It is suggested from the several investigations that casbene may serve the castor bean plant as a phytoalexin.113)

Crassin acetate (193) was shown to be the principal antineoplastic agent present in the marine invertebrates such as Pseudoplexaura parosa, P. flagelosa, P. wagenaari and P. crucis.114) The structures of ovatodiolide (194) and anisomellic acid (195) isolated from Anisomeles malabalica were determined by the spectral and chemical evidence.115)

The X-ray analysis of eupalmerin acetate (196), a diterpene lactone in the gorgonian Eunicea palmeri, and of eupalmerin acetate dibromide (197) was published.116)

A new thunbergan-type nor-isoprenoid lactone 199 was obtained from Greek tobacco. The carbon skeleton of this compound indicates that it is derived from a thunbergane precursor 198.117)
In order to clarify the absolute configuration of the tobacco thunberganoids, X-ray analysis of 5, 8-oxido-3, 9(17), 13-duvatrien-1α-ol (200) and chemical degradation of 4, 8, 13-duvatriene-1β, 3-diol (201) were performed. Correlation of the degradative product of 201 with a known tobacco constituent, solanone, established the absolute stereochemistry the carbon-1 of 201. Since the hydroxyether 200 had already been correlated with the diol 201, the absolute configuration of 200 was established. Several other components encountered in tobacco were assigned structures 202–211 by the same manner as mentioned above.²¹⁸)

(Double bonds marked with “E” are trans, although here more conveniently portrayed as cis, and those labeled “*” are of undetermined configuration.)

The structure of a new type of plant growth inhibitor extracted from immature Tobacco leaves was shown to be 4, 8, 13-duvatriene-1, 3-diol (212).²¹⁹)
The presence of 12-deoxy-phorbol (213) or ingenol (214) in several succulent Euphorbia species of Nigeria was reported. New diester of 213, that is, 12-deoxy-4β-hydroxyphorbol-13-dodecanoate-20-acetate was isolated from latex of Euphorbia coerulescens and E. fortissima. 12-Deoxy-4β-hydroxyphorbol-13-octenoate-20-acetate was isolated from E. polyacantha. A method was reported for the micro-identification of 12-deoxy—phorbol (213) and its esters having inflammatory toxicity based on thin layer chromatography-mass spectrometry.

3, 12-Di-O-acetylingol 8-tiglate (215) and some known diterpene esters of the irritant and cocarcinogenic latex of Euphorbia lactea were reported.

The crystal structures of compounds, 216 and 217, were determined by X-ray diffraction method. The structure of cotylenol, the aglycone of cotylenins, leaf grows substances produced by a fungus, was assigned on the basis of degradative and spectroscopic evidence. The structures of cotylenins A (219), B (220), C (221), D (222), and E (223) were also determined. Cotylenins F (224) and G (225) were isolated from the culture filtrate of a fungus (Cladosporium species). Cotylenin G was chemically derived from cotylenin F by treatment with a strong base.

The structure 226 of mezerein, one of the toxic components of the plant Daphne mezereum, was established by the X-ray diffraction study.

(346)
A $^{13}$C–NMR study of cis-trans isomeric vitamin A, carotenoids and related compounds was reported. The molecular mechanism of visual excitation was investigated experimentally; 11-cis- and all-trans-retinal were studied. Portulac and antheridiogen were described in the foregoing review on the growth regulating substances of plant origin.

Determination of the structure and relative configuration of crotolin A was performed using the X-ray analysis. It was shown to have a new carbon skeleton and its biogenesis was presumed.

Eremantholide A, a novel tumor-inhibiting compound from *Eremanthus elaeagnus*, was successfully isolated by utilizing countercurrent distribution, extensive chromatography and high pressure liquid chromatography. Its structure and relative configuration were substantiated as the X-ray determination. But it is not certain whether it should be regarded as a nor-diterpenoid or as a tetrahomosesquiterpenoid, although the latter possibility is strongly favored on phytochemical grounds.

Irieol A and iriediol, dibromoditerpenes of a new skeletal class from *Laurencia*, were isolated and the structures were determined by X-ray diffraction methods.

The structure and absolute stereochemistry of stemarin, a novel skeletal tetracyclic diterpene isolated from *Stemodia maritima*, were determined as by means of spectral and X-ray crystallographic analyses. The solvolysis of ent-methyl 12β-p-tolylsulfonyloxybeyeran-19-oate was investigated at room temperature in buffered acetic, formic, and trifluoroacetic acids. (See Section X.) Photochemical cleavage of the cyclopropane ring in 6, 20-epoxylythryol and the corresponding parent alcohol was described.
A new synthesis of vitamin A (238) was successfully performed. The outline is shown in Chart 11.136)

![Chemical structure of vitamin A](image)

(236) $R^1 = PhCH_2CO$; $R^2 = Ac$

(237) $R^1 = R^2 = H$

An interesting biogenetic type synthesis of cembrene type compounds was reported, in which geranyl geranic acid chloride (239) was selectively converted to the macrocyclic cembrene skeleton. The outline is illustrated in Chart 12.137)

![Biogenetic synthesis of cembrene type compounds](image)

Chart 11

Chart 12

(348)
The full paper of synthesis of rac-cembrene (240) was published. The convergent synthetic method, which employed a nickel carbonyl catalyzed coupling of a terminal allylic bromide as the important key step, is shown in Chart 13. The biosynthesis of fusicoccin (243) from [1-13C]- and [2-13C]-acetate was investigated. The positions of labeled atoms in biosynthesized fusicoccin were determined.
E. Fujita, K. Fuji, Y. Nagao, M. Node, and M. Ochiai

minded by $^{13}$C NMR spectroscopy. The results (Chart 15) were consistent with fusicoccin being formed by direct cyclization of a precursor such as geranyl geraniol pyrophosphate (242).\(^{140}\)

Measurements were described of fusicoccin-stimulated H$^+$ efflux in barley (*Hordeum vulgare*) roots when K$^+$ and Na$^+$ concentrations were varied.\(^{141}\)

In a review\(^{142}\) on the activation of Grignard reagents by transition metal compounds, the synthesis of $\delta$-pimaradiene and of beyerene from manool was cited.\(^{143}\)

A Japanese brief review related to the absolute feeding reterrent was published, in which several clerodane type diterpenes were described.\(^{144}\)

**Addendum to VI. ABIETANE DERIVATIVES**

Eleven hinokiol derivatives were prepared and their NMR investigations especially on their chemical shift variations with functional groups were carried out.\(^{145}\)

**Addendum to VII. TOTARANE DERIVATIVES**

Hallactone B (244), inumakilactone B (245), and nagilactone A were isolated from *Podocarpus polystachyus* and their structures determined on the basis of IR, NMR, and mass spectra.\(^{146}\)

(350)
Addendum to IX. KAURANE DERIVATIVES

The absolute configuration of mascaroside was determined by the X-ray crystallography as shown in formula 246.\textsuperscript{147}

REFERENCES

(3) E. Fujita, *ibid.*, 45, 229 (1967).
(22) J. de P. Campello and S. F. Fonseca, *ibid.*, 14, 2299 (1975).
(38) E. Ramstad, J. W. Powell, B. J. Wilson, S. K. Adesina, J. D. Higginbotham, and J. B. Harborne,
E. Fujita, K. Fuji, Y. Nagao, M. Node, and M. Ochiai

*Phytochemistry, 14*, 2719 (1975).


(49) A. Tahara, Y. Harigaya, and M. Onda, *ibid.*, 23, 2329 (1975).


(81) R. Evans, J. R. Hanson, and M. Siverns, *J. C. S. Perkin I*, 1514 (1975).
Chemistry on Diterpenoids in 1975. Part-II

(100) I. Snir and B. Kessler, *ibid.*, 125, 73 (1975).
(102) A. Alpi, F. Tognoni, and F. D'Amato, *ibid.*, 127, 153 (1975).

(353)
(135) A. Balmain, J. C. S. Perkin II, 1253 (1975).
(143) H. Felkin, M. Joly-Goudket, B. L. Buckwalter, I. R. Burfitt, K. Naemura, M. F. Salmon, and E. Wenkert, unpublished work.
(144) S. Hosozawa, Kagaku to Seibutsu, 13, 91 (1975).