The Chemistry on Diterpenoids in 1972

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I. INTRODUCTION

This is one of a series of annual reviews on diterpenoids chemistry. The classification is the same with that adopted in this series since 1969.

II. PODOCARPane DERIVATIVES**

The ring-B conformations of some 6,7-diacetoxy, 7-acetoxy-6-hydroxy, 6-dehydro, and 7-oxo derivatives of ring-C aromatic podocarpane derivatives were examined from a study of their NMR spectra. Birch reductions of compound 1 were investigated and the products were converted into the 13-oxo derivatives 2 and 3. The C-14 ketone 5 was also prepared from the reduced derivative 4.

Conversion of compound 6 into the synthetically more useful compound 7 was investigated. In the most favorable case, the transformation was effected in ca. 57% yield by a five-stage sequence involving hydrogenolysis of the 13-amino-12-tosylate 8 with Raney nickel.

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** See also III, ref. 29, VII, ref. 81, and IX, ref. 105.

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12-Methoxypodocarpa-8, 11, 13-trien-19-oci acid (9), its acid chloride 10, and its methyl ester 11 underwent a decarbonylation reaction on treatment with phosphoryl chloride. The products were proved to be octahydrophenanthrene 12, tetrahydrophenanthrenes 13 and 14, and the phenanthrene 15. A minor product was tentatively assigned the dimeric structure 16.12)

Reverse Ritter reaction was investigated with benzamides of steroids and diterpenoids. The benzamides, 17–19, heated in benzene with \( \text{P}_2\text{O}_5 \), underwent a reverse Ritter reaction yielding \( \text{C}_6\text{H}_5\text{CN} \) and an endo- or exo- unsaturated compound. The distribution of the unsaturated compound depended on the reaction conditions.13)

Cyclization of some 2,6-dimethyl-9-(methoxyphenyl)nona-2,6-dienes and related compounds by polyphosphoric acid was investigated to synthesize dehydropodocarpane derivatives.14) Methyl 12-methoxy-7-oxopodocarpate on nitration in conc. \( \text{H}_2\text{SO}_4 \) yielded 13-nitro-derivative (60 %) in addition to 11-nitro derivative (40 %). The photolysis of the former product was investigated.15) The syntheses of 3-acetoxo-8\( ^\beta \), 13\( \alpha \)-dimethylpodocarpan-12-one (20), the corresponding \( \Delta^{13} \)-ketone, and 3-acetoxo-8\( \beta \)-methyl-podocarpa-5, 9 (11), 13-trien-12-one (21) were carried out.16)

Enol acetylation of methyl 12-oxopodocarp-13-en-19-oate (22) was investigated. It gave mainly 23 and 24. The factor causing the unexpected thermodynamic ratio

(691)
of 3:5 noted for 23 to 24 was concluded as the result of a delicate balance between double bond stabilities and steric interactions. Kinetically controlled enol acetylation of methyl 12-oxopodocarp-8(14)-en-19-oate (25) gave 26 (60%) and 24 (25%).

The conversion of podocarpic acid (28) to an 18-norsteroid 29 was accomplished. The dimesylate 30 of one of the epimers condensed with malonic ester to give a cis-product 31, which on heating with palladized charcoal gave the trans-isomer 32. A number of derivatives of the cis-fused products were prepared. A study of the NMR spectra of the cyclization products and some of their derivatives and other data clarified their conformation.

The compound 37 was prepared via 33, 34, 35, and 36, but conversion of this compound to the corresponding acid was not successful. Birch reduction of the compound 38 was investigated, and product 39 and its hydrogenolysis product 40 were obtained. The methoxy group of compound 39 was readily displaced by acetoxy group with inversion of configuration by warming in acetic acid to give 41. Compound 40 was highly sensitive to oxygen. It was autoxidized to 42 on exposing to the air. The conformations of the 14α-methoxy-(39) and 14β-acetoxy-(41) derivatives of 3β-hydroxy-podocarp-5,8-diene were studied by means of X-ray crystallographic analysis. As a result, it was found that, in the former substance, the ring-C had an unusually flattened conformation and showed an unusual thermal behavior.
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The one-step conversion of bromo-ketone 43 to the αβ-unsaturated ketone 44 by 1,5-diazabicyclo [4.3.0] nonene-5 (DBN) in o-xylene at reflux was reported. DBN was shown to be useful for the O-alkyl cleavage of methyl esters.23)

\[
\begin{align*}
\text{(43)} & \quad \text{(44)} & \quad \text{(45)} & \quad \text{(46)} \\
\end{align*}
\]

Compound 45 was converted into compound 46, an attractive synthetic intermediate for a variety of podocarpic acid-type compounds, in a good overall yield.24)

III. LABDANE DERIVATIVES*

\[
\begin{align*}
\text{8,13-Epoxylabd-14-en-12-one (47) and its 13-epimer (48) were isolated from suncured Greek tobacco.}^{25} \text{ From the acid fraction of the oleoresin from } Araucaria excelsa \text{ were isolated commnic acid (49), sandaracopimaric acid, abietic acid, cupressic acid, and its acetyl-derivative. From the neutral fraction of the same oleoresin were isolated manool, abietinal, abietinol, torulosal, torulosol, and two new nor diterpenes. The structures 50 and 51 were assigned to them.}^{26} \\
\end{align*}
\]

\[
\begin{align*}
\text{(47) } & \quad \text{R}_1=\text{Me}, \quad \text{R}_2=\text{CH}-\text{CH}_2, \\
\text{(48) } & \quad \text{R}_1=\text{CH}-\text{CH}_2, \quad \text{R}_2=\text{Me} \\
\end{align*}
\]

The tetrahydro-derivative 52 of the naturally occurring diterpene, 7α-hydroxy manool, was synthesized.27) Utilization of manoyl oxide and related compounds for the preparation of compounds with ambergris-type odors was investigated. The acetal 53 prepared from sclareol was shown to have an ambergris-type odor of strength comparable to that of highly odoriferous acetal 54. Attempts to convert 2-oxomanoyl

* See also VI, ref. 79.
oxide 55 and manoyl oxide into the ethers 56 and 57 still retaining the original cyclic ether groups were also published.29)

Lambertianic acid (58) synthesized starting from podocarpic acid. The central intermediate, diester-ketone 59, was obtained by ozonolysis and hydrogenation, and the exocyclic methylene group in ring B was generated via a Reformatsky reaction. The furan ring was attached by nucleophilic attack of 3-lithiofuran and the 12-oxygen atom was removed by mesylation of the alcohols 60 and Li-liquid ammonia reduction.29)

The synthesis of marrubiin (68) was achieved starting from the keto lactone 64 which was prepared stereoselectively from the known keto ester 61 via 62 and 63. The compound 64 on reaction with Li acetylide followed by reduction gave 65, which gave 66 on treatment with PBr₃ in pyridine. The bromide 66 was converted into furanoepoxide 67 by a reaction with 3-furanyl lithium followed by epoxidation. The final step, conversion of 67 into marrubiin (68) was achieved by reduction with lithium in ethylamine.29)

Dehydration of sclareol 8-acetate with POCl₃-pyridine yielded a mixture of acetates of iso- and trans-abienols, whereas pyrolysis of the 13-acetate by distillation proceeded through an ion pair forming mixed isoabienol, trans-abienol, 13-epimanoyl oxide and manoyl oxide (69).31)
A bicyclic C-13 carbonium ion 72 was generated in vitro from manool (70) and \(\Delta^{13}\)-manool (71) and found to give, in refluxing AcOH, a 1:1 mixture of \(\Delta^{13}\)-manool acetate and olefins. The ring closures between C-13 and C-17 and between C-15 and C-17 were observed. The former cyclization gave approximately equal amounts of tricyclic \(\alpha\)-vinyl isopimamic and \(\beta\)-vinyl pimamic \(\Delta^1\), \(\Delta^2\), and \(\Delta^{14}\) dienes together with the products of backbone rearrangement. Under refluxing formic acid, formation of labdatrienes was precluded and yields of the initially cyclized pimaradienes and isopimaradienes, the backbone rearranged products and the product cyclized between C-15 and C-17 increased. The initial dienes and backbone rearranged products were interconverted by the reaction conditions showing that backbone rearrangement is reversible. A tetracyclic product, hiban-14\(\alpha\)-yl-formate, was also isolated and was formed quantitatively when the product formed by the cyclization between C-15 and C-17 possessing \(\Delta^8\) and \(\Delta^{13}\) was subjected to the reaction conditions. Deuterium labelling of \(\Delta^{13}\)-manool at C-14 showed that hiban-14\(\alpha\)-yl-formate was formed via such a carbon skeleton. Thus, the biogenesis of tetracarbocyclic diterpenes was considered.32)

\[15-3^H\]ent-Labda-8(17), 13-dien-15-ol pyrophosphate was found to be specifically incorporated into ent-13-epimanoyl oxide (73) by Gibberella fujikuroi.33)

Desoxytaondiol methyl ether (74), a derivative of taondiol (75) previously isolated from Taonia atomaria, was synthesized from manool (70) by two steps of reactions.34)

**IV. CLERODANE DERIVATIVES**

The absolute stereochemistry of maingayic acid was established as 76 by correlating it with hardwickiol acetate (77). The furano-olefin 78 derived from maingayic
acid was identical with the product obtained by hydrogenation of 77 in ethanol-
triethylamine over palladium charcoal at 20°.35)

Clerodendrin A (79) and B were isolated from Clerodendron tricotomum. They
showed the antifeeding activities for the tobacco cut worm. Clerodendrin B has a
planar structure of 7,8-dihydro-derivative of clerodendrin A, but its stereochemistries
at C-8, -9, -11, -13, and -16 are unknown.36) From Conyza ivaefolia (Compositae),
a clerodane-type diterpene, hautriwaic acid (80), which had been isolated from
Dodonea attenuata by Jefferies and Payne,37) was isolated.

Acidic components of Solidago altissima roots were methylated with diazomethane
and repeatedly chromatographed on silica gel to give two oily and one crystalline bitter
principles. Their structures were elucidated as methyl 6-angeroyloxy- (81), 6-tygroyloxy-
(82), and 2-oxokolavenate (83).39) Isolation of columbin from Spirospernum
penduliflorum was reported.40) 11-Dehydro-ent-hardwickiic acid (84) and ent-hard-
wickiic acid (85) were isolated from Croton oblongifolius.41)

From Teucrium chamaedrys were isolated four bitter diterpenes, and their func-
tional groups were characterized.42) The planar structure was assigned to stachy-
solone, a bitter substance from Stachys annua, on the basis of spectral and chemical
evidence.43) Subsequently, the stereochemistry of stachysolone was investigated and
formula 86 was given to it.44)
On the basis of the X-ray crystallographic study of 2-dehydro-3-bromo-tetrahydrodiosbulbin-A (87), the structure of tetrahydrodiosbulbin-A, diosbulbin-A, -B, and -C were revised to 88, 89, 90, and 91, respectively.45)

V. PIMARANE AND ISOPIMARANE DERIVATIVES*

The crystal structure of 12β-hydroxysandaracopimaric acid was determined from three-dimensional data collected on a single-crystal diffractometer with CuKα radiation.46) Three nor-diterpenes, 19-norpimara-8(14),15-dien-3-one (92), 19-norisopimara-8(14),15-dien-3-one (93), and 19-norisopimara-7,15-dien-3-one (94) were isolated from the bark of Pinus silvestris. Moreover, the following diterpenoids were characterized mainly by TLC and GLC: pimaral, isopimaral, dehydroabietal, pimaric acid, isopimaric acid, levopimaric acid, palustric acid, dehydroabietic acid, abietic acid, and neoabietic acid.47) Two new diterpenes, ent-pimara-8(14),15-dien-19-ol and ent-pimara-8(14),15-dien-19-al were isolated from Aralia cordata. Autoxidation of the latter was described.48)

Syntheses of 95, 96, and 97, which were regarded as potential intermediates for the synthesis of friedo-pimarane type diterpene, were carried out.48-49)

A new diterpene, 3β-hydroxysandaracopimaric acid (98), was isolated from Juniperus rigida.50) The structure of lagascatriol isolated from Sideritis angustifolia was proved to be 99, on the basis of NMR spectral investigations and some reactions.51)

* See also II, ref. 13, III, ref. 26, VI, refs 79 and 80, VII, ref. 83, and X, ref. 144.
Autoxidation of isopimaradienal was investigated and the formation of hydroperoxides was found. Additionally, a mixture of norditerpenoid hydrocarbons 100 and 101 were formed. Analogous results were obtained for dehydroabietinal and epititorulosal.52)

[Chemical structures and text]

Carbon-13 NMR spectroscopy of pimaradienes was investigated. The chemical shift data for the pimaradienes, 102, 103, 104, and 105, were utilized for the determination of the otherwise difficultly assignable ring C conformation of the 48I"-pimaradienes (105) as well as for the elucidation of the biosynthesis of the virescenosides, fungal isopimaradienic glycosides.53' These diterpene glycosides were isolated as the metabolites of mushroom Oospora Virescens. The biosynthesis of aglycones 106 and 107 was uncovered by carbon-13 NMR spectroscopy. The 13C natural abundance NMR spectra of the aglycone alcohols, 106, 107, and 108 and their double bond isomers, 109 and 110, obtained by acid hydrolysis of the glycosides, were recorded and their chemical shifts collected. Assignment of the δ values was then carried out.

Addition of sodium [1-13C] acetate to the mushroom culture medium, isolation of virescenoside A (111), hydrolysis to isovirescenol A (109), and inspection of the CMR spectrum of the latter revealed strong signal enhancement of the carbons depicted in 112. Similar treatment of the culture with sodium [2-13C] acetate, isolation of virescenoside A (111) and B (113), conversion into isovirescenols A (109) and B (110), and perusal of the CMR spectra of the 13C-enriched alcohols showed intense signal enlargement of the carbons portrayed in 112. These results fit the present theory of the terpene biosynthesis.54)
Two novel pimarane diterpenes LL-S491\(\beta\) (114) and \(-\tau\) (115) were isolated from fermentation of the fungus *Aspergillus chevalieri* (Lederls culture S491). LL-S491\(\beta\) displayed significant antibacterial activity against certain gram-positive organisms and LL-S491\(\tau\) exhibited antiviral activity against *Herpes simplex*. Both compounds possess strong antiprotozoal activity against *Tetrachymena pariformis*. The structures of these antibiotics were elucidated.\(^{55}\)

Two short reviews on chemistry of pimaranes were published by Indian\(^{56}\) and Japanese authors.\(^{57}\)

**VI. ABIETANE DERIVATIVES*\(^{\,*}\)**

The crystal structure of levopimaric acid (116) was investigated. The acid was found to form a dimer by hydrogen bonding between the carboxyl groups of two independent molecules in the asymmetric unit.\(^{58}\)

The hot tube pyrolysis of dehydroabietic acid (117) at 400–500° was found to produce as major products the three possible ring A olefins, 118, 119, and 120 resulting from the elimination of the carboxylate moiety.\(^{59}\) The pyrolysis of abietic acid (121) and levopimaric acid (116) under identical conditions was found to yield ring-A olefins, isomerized products, dehydrogenation product 117, and an elimination product *i.e.* deisopropyldehydroabietic acid (122). A mechanism was suggested for explanation of the formation of 122.\(^{60}\) (Chart 1)

* See also II, ref. 13, III, ref. 26, V, ref. 47, VI, ref. 80, and VII, ref. 83.

\(^{\,*}\) Sec also II, ref. 13, III, ref. 26, V, ref. 47, VI, ref. 80, and VII, ref. 83.
Conversion of abietic acid (121) to steroids was attempted and syntheses of the ketone compounds, 123 and 124, were carried out. These compounds were regarded as the important intermediates in the synthesis of the skeleton of steroid antipodes.

Coleon D, a new orange red diterpenoid hydroquinone, was isolated from the yellow glands on the leaves and inflorescences of Coleus aquaticus (Labiatae). The structure was determined as 125, which corresponded to a tautomer of coleon C 126. Another new, very labil, deeply red colored quinone methide, coleon E, was isolated from the glands on the leaves of Coleus barbatus, C. kilimandschari, and a Coleus species, all of East African origin, and structure 127 was assigned to it.
Miltirone (129), a novel tricyclic diterpenoid quinone, was synthesized via 6-isopropyl-7-methoxy-1-tetralone (128). Methyl dehydroabietate (131) was prepared in a single step by dehydrogenation of methyl levopimarate (130) with EtO₂C·N=N·CO₂Et at 25°. A new yellow diterpenoid, lycoxanthol, was isolated from *Lycopodium lucidulum*, and its structure was suggested to be 132.

Structures were deduced for the products resulting from the KMnO₄ and OsO₄ oxidation of levopimaric acid (116). The major product of KMnO₄ oxidation was an epoxidodi hydroxy carboxylic acid 133. The products from OsO₄ oxidation of methyl levopimarate (130) were diols, 134 and 135, and tetraol 136. The preparation of other enedials, epoxydiols, and tetraols derived from levopimaric acid was also reported.

It was found that a photostationary state of 50:50 exists between palustric acid (137) and the trienes 138c and 138t. The enhanced ring closure was explained on conformational grounds, noting that the isopropyl group destabilizes the transoid rotamer 138t and hence increases the concentration of the cisoid rotamer 138c which has the correct geometry for efficient ring closure. By evaluation of all related data, it was established that the photostationary state between diene and triene was controlled by the conformation of the triene.

Benzene solutions of levopimaric acid, abietic acid, dihydroabietic acid, and methyl dehydroabietate were pyrolyzed at 800° on Vycor glass to yield tars containing the following general spectrum of products: toluene, styrene, indene, naphthalene, 2-methylnaphthalene, 2-vinylnaphthalene,acenaphthylene, phenanthrene, fluorene, and 2-phenyl naphthalene. The pyrolysis of methyl dehydroabietate in the absence of benzene indicated that toluene, styrene, indene, fluorene, and 2-phenyl naphthalene were the result of secondary reactions of pyrolysis products with phenyl radicals. Analysis of the products resulting from the pyrolysis of retene, under the same conditions, indicates that the high yield of naphthalene-related products obtained in the resin acid pyrolyzates must arise from A-ring cleavage in the parent molecule before complete aromatization occurs.

Dehydroabietylamine derivatives, e.g. 139–142, were prepared in high yields by reduction of the corresponding amide derivatives with LiAlH₄. Analogously amine 143 was obtained from the corresponding amide.
Amber samples of different provenance were investigated by electron impact and field ionization mass spectrometry. Whereas electron impact mass spectra were not specific enough, field ionization spectra enabled one to identify amber from Baltic, Sicilian, Canadian, and Libanese areas. Very often the fragment peaks at m/e 302 and m/e 604 were observed. The former corresponds to a resin acid of abietic acid type (C_{20}H_{30}O_3) and the latter to the diabietic acid type 144^{71}.

rac-Royleanone (146) was synthesized from 5,7,8-trimethoxy-1-tetralone via podocarpene derivative 145^{72}.

The oxidation of methyl 7-oxodehydroabietate (147) with perbenzoic acid and treatment of the crude product with methanol containing conc. HCl afforded a mixture of lactone 148, quinone 149, hydroxy ester 150, and hydroxyquinone 151. The intramolecular cyclization of half acid 152 derived from 150 gave two ketoesters 153 and 154. The compound 154 was converted into 11-methoxydehydroabietane (155)^{73}.

Friedel-Crafts reaction of methyl 12-bromodehydroabietate (156) with acetyl chloride afforded methyl 13-acetyl-14-bromo-12-isopropyldehydroabietate (157),
its cis-isomer (158), and methyl 12-acetyldehydroabietate (159). Conversion of 157 into sempervirol (160) was carried out and the absolute configuration of sempervirol was assigned.\textsuperscript{75}

Benzonilidene compound 161 underwent rearrangement to 162 with 1,2-methyl migration and \textit{vice versa}. Using the rearrangement, selective substitution at C-1 of dehydroabietic acid derivative was accomplished to give 163.\textsuperscript{75}

Nitration of methyl 7-oxodehydroabietate (147) with fuming HNO\textsubscript{3} and conc. H\textsubscript{2}SO\textsubscript{4} (10:1) at 0–5° gave nitro compounds 164 and 165.\textsuperscript{76}

From the fresh roots of \textit{Euphorbia Jolkini} were isolated two new diterpenoids, jolkinolides A and B. Their structures were elucidated to be 166 and 167, respectively.\textsuperscript{77} When a CH\textsubscript{2}Cl\textsubscript{2} solution of levopimaric acid (116) was dispersed in 96% H\textsubscript{2}SO\textsubscript{4} (5–10°), clear light orange solution of cation 168 was obtained. On quenching the cation solution in iced aq. Na\textsubscript{2}CO\textsubscript{3}, a near quantitative recovery of abietic acid resulted. Cation 168 at 25° (2 hours) in H\textsubscript{2}SO\textsubscript{4} underwent smooth rearrangement to 169 as evidenced by its UV spectrum and NMR spectrum. Quenching the cation 169 gave an unstable dienoic acid 170 in 80% yield and was purified through its methyl ester. The dienoic acid 170 regenerated cation 169 on dissolution in 96% H\textsubscript{2}SO\textsubscript{4}.\textsuperscript{78}
A brief review of the chemistry of the conifer order Pinales was presented. Some chemical relationships of taxonomic interest were pointed out. Unpublished results on the bark extractives of *Pinus sylvestris* and *Picea abies* and on the constituents of the oleoresin of the latter species and *Larix decidua* were briefly reported. This review contains not only abietane types, but strobic acid, pimarane types, labdane types, and also macrocyclic diterpenoids of Pinales species. Another review on the amber was published. The provenance, the participation of various resin acids for the formation of amber, chemical components, and identification methods are described.

**VII. TOTARANE DERIVATIVES**

Totara-8,11,13-trien-7-one (171) was treated with conc. \( \text{H}_2\text{SO}_4 \) and \( \text{HNO}_3 \) at room temperature to give a nitro lactone derivative 172. The similar fact was observed on the nitration of podocarpane derivative 173, which gave a usual nitro product 174 and nitro lactone aldehyde 175.

A lactone derivative 176 was extracted from the leaves of *Podocarpus saligna*. Totarol, 3-oxototarol, 1,3-dioxototarol, sugiol, sandaracopimmaric acid, isopimaric acid, and xanthoperol were isolated from *Juniperus conferta*. 
The plant-growth inhibitory activities of 12 kinds of compounds which were related to podolactones were determined using a pea-stem growth system. Podo-lactone E, isolated from Podocarpus neriifolius was the most active inhibitory compound. The structure 177 was assigned to this substance mainly on the basis of the NMR investigation. This substance is very likely a biogenetic precursor of inumakilactone B, which can be formed by epoxidation of the 7,8-double bond: hydration of the side chain of the latter compound may then lead to inumakilactone A.

The stereochemistry of nagilactone A and B was established by the spectral analyses and the X-ray method. The absolute configurations of both substances were also proposed as shown in 178 and 179, respectively. The structures of two new norditerpenoid dilactones, nagilactone E and F, were proposed as 180 and 181. A dual biological activity of nagilactones (inhibitory and promotive) for plant growth was also reported.

Further norditerpenoids of Podocalpus macrophyllus were investigated. The structures of inumakilactone E and inumakilactone A glucoside were elucidated as 182 and 183. The latter was shown to be a potent inhibitor of the expansion and division of the plant cells.

VIII. CASSANE DERIVATIVES

Syntheses of racemic, isomeric deoxo-4,14-didemethylcassaic acid derivatives, 185 and 186, were carried out via 184. From 185 and 186, some derivatives were synthesized.
An aldehyde isolated from the Venezuelan plant *Expelitia weddeli* was identified by its crystal structure analysis to be *ent*-15-kauren-19-al (187). Two diterpenes, leucanthol (188) and isoleucanthol (189) were isolated from *Sideritis leucantha*, and their structures were determined.

Definitive evidence concerning the revised structure (190) for grandiflorenic acid, extracted from the resin of *Espeletia grandiflora*, was provided. The resin also contained the known kaurene-type diterpenes, *ent*-16-kauren-19-oic acid, *ent*-16-kauren-19-al, and *ent*-16-kauren-19-ol.

On the basis of chemical and spectroscopic evidence, the structure and absolute configuration of the highly oxygenated diterpenes, lasiokaurin and lasiodonin isolated from *Isodon lasiocarpus* were shown to be (191) and (192), respectively.

A sequence of sterically controlled reactions from enmein (193) gave naturally occurring isodotricin (194), and it established the absolute stereochemistry at C-16.

A new metabolite of *Gibberella fujikuroi* was isolated and shown to be 3β, 7β-dihydroxykaurenolide (195). It is the first time that the C-3 hydroxylated compound was isolated from the metabolite of this fungus. It suggests an alternative biosynthetic route to the gibberellins, in which 3-hydroxylation precedes ring contraction.

The fact that ring A of the brosylate (196) of 7β-hydroxykaurenolide is distorted

* See also X, ref. 145 and XI, ref. 173.
from ideal chair geometry while rings B and C adopt distorted twisted boat conformations was recognized by its three-dimensional X-ray analysis.96)

Six kinds of plants belonging to *Isodon* genus were checked for diterpenoid component. *I. longitubus* contained four known diterpenoids, nodosin (197), isodocarpin (198), oridonin (199), and lasiokaurin (191). Six new diterpenes were isolated and named isodomedin (from *I. shikokianus var. intermedius*), kamebanin, mebadonin (from *I. kameba*), inflexin (from *I. inflexus*), umbrosin (from *I. umbrosus*), and effusin (from *I. effusus*). Molecular formulae and spectral data indicated that all these compounds are tetra-cyclic diterpenoids.97)

A new diterpene, stenolobin, was isolated from *Viguiera stenoloba* and the structure was elucidated as 200.98) Calliterpenone (201) and calliterpenone monoacetate (202) were isolated from the aerial parts of *Callicarpa macrophylla* and their structures and stereochemistry were reported on the basis of spectral data and their conversions to ent-17-norkaurane.99)*

A new sulfated glycoside, carboxyatractyloside (203) was isolated from the rhizomes of *Atractylis gummifera*. The structure of the aglycone, carboxyatracylicigenin (204), was determined by means of spectroscopic as well as chemical data and confirmed by correlation with the known atractyligenin (205). The structure of the glycoside was determined by correlation with atractyloside (206).100)

Six diterpenes, foliol (207), isofoliol (208), sidol (209), isosidol (210), linearol (211), and isolinearol (212), were isolated from *Sideritis leucantha*. *S. linearifolia* yielded foliol (207), sidol (209), and linearol (211) only.101)

* Recently, however, the structure of calliterpenone was revised to 13ß-kauran-3-one-16ß,17ß-diol (A) by Ahmad and Zaman.102) The correctness of the structure A was reconfirmed by the joint work103) of the author's (E. F.) group and Chatterjee's group.
Total syntheses of a kaurane derivative 214 and related compounds which are potential intermediates for the synthesis of highly oxygenated diterpenes such as grayanotoxins, were accomplished from 213.104

Oxidative degradations of phyllocladene (215) and isophyllocladene (216) were carried out. Several routes from phyllocladene (215) into the diacid 218 via norketone 217 were demonstrated. On a series of reactions including ozonolysis, isophyllocladene (216) was converted into podocarp-8-(14)-en-13-one (219), an optically active relay which is useful in syntheses. It is of interest that the ozonide 220 of isophyllocladene was isolated and characterized.105

An interesting hydrolysis of glucoside bond in stevioside (221) by a soil bacterial strain (YSB-9, unidentified) was reported. It gave steviolbioside (222) as a major product and steviol (223) as a minor.166
Some chemistry concerning the epoxides of phyllocladene (215), isophyllocladene (216), and kaurene-phyllolocadene type compounds was described. The products from, and the effect of solvent on the ring-opening of 15α, 16-epoxyphyllocladane (224) and of 16α, 17-epoxyphyllocladane (225) with boron trifluoride as well as other Lewis acids were examined. Treatment of ent-15β, 16-epoxykaurane (226) with boron trifluoride-ether complex results rearrangement, giving ent-atisan-15-one (227). Photo-oxygenation of phyllocladene (215) and isophyllocladene (216) was also studied.107

The secondary hydroxy-group of sidoridiol (228) was confirmed as being in the 7- rather than the 12-position by conversion of the former into ent-7-oxokaur-5-en-18, 6-olide (229).108 Some reactions in ring D of 13β-kaurane (phyllolocadane) derivatives were reported. Metal hydride reduction of 13β-kaur-16-en-15-one (230) afforded tetrahydro-derivative 231, but none of the expected 1,2-reduction product 232. Treatment of 13,8-kaur-16-en-15α-ol (233) with aqueous acid in methanol yielded a dimeric ether 234 in addition to 17-hydroxy-(235) and 17-methoxy-13β-kaur-15-ene (236).109

The enolization-ketonization of the ent-kauran-15-ones and 13β-kauran-15-ones was reported. At temperature below 100° the rates of enolization of ent-kauran-15-one (237) and 13β-kauran-15-one (238) were much greater than those of the 16S-epimers, and the enols were exclusively ketonized to the 16R-epimers. Reasons for this kinetic control were discussed in terms of steric hindrance, torsional strain, and stereo electronic factors.110
Enmein (193) was converted into ent-15-kaurene (239), ent-16-kaurene (240), and ent-kaurane (241). Thus, acyloin condensation of lactone ester 242 derived from enmein (193) by several steps afforded a key intermediate 243. On Jones oxidation followed by Huang-Minlon reduction, diol 243 gave 239, 240, and 241, via keto aldehyde 244. On the other hand, Nagata's modification of Wolff-Kishner reduction on 244 afforded ent-kaurane (241) as a sole product. Hydrogenation of the double bond during the Nagata's modification of Wolff-Kishner reduction was studied in detail using ent-16-kaurene (240) as a reference compound and the possible mechanisms were discussed.

The stereochemistry of hydroboration, osmylation, and epoxidation of some kaur-6,7-enes was investigated. The attack of the reagents takes place exclusively from $\beta$-side of the molecule to give a variety of substances suitably functionalized for study in gibberellin biosynthesis.

rac.-Steviol (223), tetracyclic diterpene with a substituent at the bridgehead C-13 position, was synthesized starting from the known keto ester 245 through the sequence shown in Chart 2. Conversion of 246 into steviol (223) had been accomplished by the same authors in 1971.
Kaurenoic acid (247) and epimeric hydroperoxides 248 and 249 were obtained by autoxidation of *ent*-kaur-16-en-19-al (250). Extensive studies on autoxidation of *ent*-16-methoxy-kauran-19-al (251) were carried out and a suggestion that some 4-hydroxynorditerpenes isolated from natural sources so far are probably artifacts was provided.\(^{116}\)

\[
\begin{align*}
(247) & : R^1 = \text{Me}, R^2 = \text{CO}_2\text{H} \\
(248) & : R^1 = \text{OOH}, R^2 = \text{Me} \\
(249) & : R^1 = \text{Me}, R^2 = \text{OOH} \\
(250) & : R^1 = \text{Me}, R^2 = \text{CHO}
\end{align*}
\]

Diol 252 derived from enmein (193) was transformed into enmein through the sequence of the reactions shown in Chart 3. Thus the first total synthesis of enmein was accomplished since the diol 252 was synthesized from 2,5-dihydroxynaphthalene.\(^{117}\)
The copper-catalyzed decomposition of the diazomethyl ketones 255 and 256 followed by simple chemical reactions offered a new method for the preparation of tricyclic compounds 253 and 254 containing the 3,2,1- and 2,2,2-bicyclooctane ring systems which are envisaged as intermediates in a "BC+D+A" total synthesis of tetracyclic diterpenoids.\textsuperscript{118}

Very rare example of bridgehead enolization was demonstrated in \textit{ent}-kaurene derivative.\textsuperscript{119} The deuterated ketone 257 with 36-47\% deuterium at C-14 and virtually 100\% deuterium at C-13, prepared from \textit{ent}-beyer-15-ene (258) through a series of reactions, was shown to lose almost all of deuterium at C-13 on treatment with \textit{t}-BuOK and \textit{t}-BuOH at 172° for 72 hr. in a sealed tube.

The preparation from \textit{Gibberella fujikuroi} of a cell-free system that converts mevalonate into \textit{ent}-kaurene (240) was reported. The system was used to show that a pimaradiene intermediate is not involved in the biosynthesis of \textit{ent}-kaurene by \textit{Gibberella fujikuroi}. However, an enzyme-bound pimarane with, for example, a stabilized C-8 carbonium ion system or the direct cyclization of pyrophosphate 259 illustrated in Chart 4 are possible alternatives.\textsuperscript{120}

As a preliminary experiment of the biosynthesis, changes in the quantity of major diterpenoids, enmein (193), oridonin (199), and isodocarpin (198) were examined every ten days by GC and GC-MS. Enmein (193) and oridonin (199) were found to increase markedly in June and July.\textsuperscript{121}

Mass spectra of five kaurane derivatives, 260-264, were studied by Russian workers.\textsuperscript{122}
An interesting method was presented by which the specific radioactivity of [14C]-labeled compounds can be determined using MS data for GLC-MS. The specific activity of [14C]-labeled ent-kaurene (240), ent-7α-hydroxykaurenoic acid, ent-kaurenoic acid, and gibberellin A12-aldehyde were determined by this method. These compounds were thus shown to be derived from 2-[14C]-MVA without significant dilution of the label in a cell-free enzyme system from *Cucurbita pepo*. Mass spectra of [17-13C] kaurene, [17-13C]-6-hydroxykaurene, and [17-13C]-kaurane were reported and discussed.

Interproton allylic spin-spin coupling involving exocyclic groups was extensively studied for 55 compounds including lasiokaurin (191) and 1-epi-enmerol (265). The J35,16 values for the stereoisomeric ent-kauran- and 13,9-kauran-15-ols indicate a twist envelope conformation for ring D in all except the (16S)-15,9-ols. The chemical shifts of the C-15 protons confirm the stereochemical assignments.

Lactone rings in 266, 267, 268, and 269 were shown to exist in chair conformation by ORD curves and solvent shift in NMR spectra.

Eight A-nor-B-homo-kaurane type diterpenes were isolated. They are gray-anotoxins-XII (270), -XIII (271), -XIV (272), and -XV (273) from *Leucothoe grayana*, lyoniol-D (274), from *Lyonia ovalifolia var. elliptica*, rhodojaponins-V (275), -VI (276), and -VII (277) from *Rhododendron japonicum*.
Grayanotoxin II (278) was converted to 20-nor-kaurane derivatives (279) and (280) through a sequence shown in Chart 5.\textsuperscript{133}

![Chart 5](image)

Partial synthesis of grayanotoxin-II (278) from its degradation product 281 was reported.\textsuperscript{134} The route is shown in Chart 6.

![Chart 6](image)

The compounds 283 and 284 with grayanotoxin skeleton were prepared by photochemical reaction of the synthesized compound 282 and its C-14 epimer.\textsuperscript{135}
Chemistry on Diterpenoids in 1972

The first isolation of anthraditerpenoid, leucothol A from *Leucothoe grayana* was reported and the structure was determined as 285 by means of X-ray crystallographic analysis. Other three diterpenoids in this class were additionally found in this year. They are leucothols B (286), C (287), and D (288).

On the basis of the structure 289 of the product of a reaction between O.O.O.O-tetraacetylanopteryl alcohol and methyl iodide, the parent alkaloid, anopterine, isolated from *Anopterus macleaganus* and *Anopterus glandulosus* was shown to have the structure 290. The structure 289 was determined by an X-ray analysis.

An approach to the total synthesis of songorine (291) has been tried by Wiesner’s group. A ketoester 292 was stereoselectively converted to a crucial intermediate 293 which was further converted to the penta cyclic keto lactam 294 by a series of reactions. The syntheses of diketones 295 and 296 from phenol 297 had been reported by Wiesner et al. in 1970. In view of the considerable synthetic value of these ketones an X-ray analysis of 295 was carried out to confirm their structure.
The structures of seven new diterpenoids 298–304 from the root wood of *Erythroxylon australe* were assigned on the basis of chemical and spectroscopic evidence. Two of them were isolated as isopropylidene acetals, 303 and 304, by treatment with acetone and copper sulfate. Six known compounds including *ent*-15-beyerene (306) were also isolated.

The crystal structure of the *p*-bromobenzenesulfonate of *ent*-beyeran-3β ol (305) was elucidated by three-dimensional X-ray method. In (305), rings A, B, and C have chair conformations.

A recently isolated new naturally-occurring compound of a 12-oxo-beyer-15(16)-ene system was confirmed to undergo a double 1,2-rearrangement across the 12, 13-single bond in acid medium, because the structure of the *p*-bromo-benzoate of the acid rearranged compound was established as 308 by X-ray crystal structural analysis. Namely, 307 induced high yield rearrangement to 309 with various acids. Furthermore, addition of acid to an acetic acid-acetic anhydride solution of the dihydro-derivative 310 afforded 311. The easy rearrangement of this system was proposed as indicated in the Chart 7.
From biosynthetic study of diterpenes in *Beyeria leschenaultii*, beyerene and beyeren-19-ol was indicated to serve as precursors of beyerol, 17,19-dihydroxybeyer-15-en-3-one and the 3,4-secobeyerene acid 312 but only beyerene was incorporated into 6β,17-dihydroxybeyer-15-en-3-one, the major component. The significance of beyerene and beyeren-19-ol as precursors of 312 is discussed with reference to possible mechanism for its formation.¹⁴⁹

Synthesis of (+)-14-hibaone (317) from 4604'-podocarpen-13-one was accomplished as shown in Chart 8, which included a photochemical reaction with dichloroethylene and a direct conversion of the tetracyclic epimeric alcohols 313 and 314, precursors of the biogenetic intermediate 315 postulated by Edwards, into 14α-hibyl acetate 316.¹⁵⁰

---

**Chart 7**

**Chart 8**

---

(717)
Erythroxydiol A (318) was synthesized *via* a route in Chart 9\(^\text{114}\) from the steviol methyl ester synthesized already.

![Chemical reaction diagram]

**Chart 9**

**XI. GIBBERELLANE DERIVATIVES**

From immature seeds of *Wisteria floribunda*, gibberellins A\(_{18}\) and A\(_{23}\) were isolated.\(^{181}\) Gibberellins A\(_9\) and A\(_{13}\) were isolated from *Enhydra fluctuans* and identified on the basis of m.p., m.m.p., IR, MS and co-chromatography.\(^{182}\)

A new naturally occurring tetrahydrogibberellin A\(_9\) was isolated from the leaves of *Sonneratia apetala*,\(^{183}\) but the identification was questioned by MacMillan and Takahashi\(^{184}\) on the basis of the reported m.p., UV, and NMR spectra. Therefore, this gibberellin, m.p. 280–285°, was re-isolated and conclusively identified\(^{185}\) by direct comparison with tetrahydrogibberellin A\(_3\), m.p. 285–290°.

Glucosyl esters 319 and 320 of GA\(_{37}\) (321) and GA\(_{38}\) (322) together with free GA\(_1\) and glucosyl ester of GA\(_4\) were isolated from mature seeds of *Phaseolus vulgaris*.\(^{186}\)

Full paper about structure of gibberellin A\(_{23}\) (323) isolated from the immature fruits of *Lupinus luteus* was published.\(^{187}\) A new gibberellin, GA\(_{36}\) (324) was isolated from the culture filtrates of *G. fujikuroi*. Confirmation of structure for GA\(_{36}\) was obtained by reduction with sodium borohydride to GA\(_{37}\) (326).\(^{188}\)
A short review on recent progress in chemistry of gibberellins was published in Japanese.\(^{159}\)

Stereochemistry at C-16 of dihydrogibberellin A\(_1\) methyl ester (327) and its 16-epimer was elucidated\(^{160}\) by NMR analysis employing a shift reagent, Eu(thd)\(_3\), or Eu(fod)\(_3\).

Spectroscopic methods for assignment of C-9 stereochemistry in gibbanes, 328 and 329, were presented. Namely, in the C-9\(\alpha\) gibbanes the respective C-6 methylene protons resonate at higher field than those of the isomeric C-9\(\beta\) gibbanes. In gibban-16-ones having ester functionality at C-4 or C-6 there is a tendency for C-9\(\alpha\) isomer to exhibit C-16 carbonyl absorption in the infrared near 1740 cm\(^{-1}\) whereas C-9\(\beta\) isomers absorb near 1730 cm\(^{-1}\).\(^{161}\)

The photochemistry of GA\(_3\) derivative 330 in ethanol, isopropanol and dioxan was investigated. In all three cases the following reaction types were found; (a) photoreduction of the \(\Delta^1\)-double bond leading to the saturated ketone 331; (b) C-addition of a solvent molecule to this bond leading to the corresponding 1-substituted ketones 332, 333, or 334; (c) photoaromatization of ring A; (d) extensive cyclodimerization leading to the products of type 335. In EtOH and iso-PrOH the formation of the O-adducts 336 and 337 also takes place.\(^{162}\)
The configurations at C-1 of gibberellin A₃ epoxy derivative 338 and its EtOH photoaddition products, 339 and 340, were determined on the basis of their NMR spectra and by comparison of their CD curves with 341, 342, 343, and 344.¹⁶³

Gibberellanes in which ring A is aromatic react with DDQ giving allylic carbanion ions (via α-enes) which then undergo Wagner-Meerwein rearrangement; in 13-hydroxy-compounds such as 345, the 13,16-bond migrates to C-12 to give a 13-keton 346, whereas in 13-deoxy-gibberellanes such as 347 or 348, the 8,15-bond migrates to position 9 to give a 6,8-ene such as 349 or 350,¹⁶⁴ as shown in Chart 10.

Functionalization of non-activated C-H bond by photolysis of some nitrones was studied. The nitrone 351 derived from enmein (193) in 14 steps was photodecomposed under various conditions, and the products 352 and 353 were obtained in a favorable yield. The possible mechanisms (a and b) were presumed as shown in Chart 11. The compound 352 was then converted into gibberellin A₁₅ in 6 steps.¹⁶⁵
Partial synthesis of gibberellin A₃ by selective reduction of the hindered 10-carboxy-group in gibberellin A₁₃ was reported,¹⁶⁶ as shown in Chart 12.

Gibberellin-A₃-O(3) β-D-glucopyranoside (354) was prepared from gibberellin A₃ methyl ester and α-acetobromoglucone followed by demethylation and deacetylation.¹⁶⁷

An aromatized ring-A gibberellane derivative 355 was synthesized from terracinoic acid (356) which was prepared from terramycin.¹⁶⁸

A stereospecific synthesis of compound 357 suitable for elaboration to gibberellin A₄ was reported, as shown in Chart 13. However, in preliminary investigation, it was shown that the compound 358 derived from 357 readily undergoes decarboxylation and oxidation to 359 under very mild conditions.¹⁶⁹
A useful synthetic route to the epimeric diacid derivatives 360 and 361 was provided by selective metalation and carbonation of N-methylamide 362, as shown in Chart 14. The applicability of the Birch reduction to the conversion of the methoxy acid 363 to either enol ether 364 or the keto acid 365 was also demonstrated.10) Tricyclic bridged compounds 366 and 367 related to gibberellinic diterpenes were synthesized.11,12) Full report on new synthetic routes to tetracyclic bridged-bicyclo[3.2.1]octane intermediates 368, 369, and 370 by intramolecular alkylation reactions through α-diazomethyl ketones of hydroaromatic γ,δ-unsaturated acids was published.12)
This route is shown in Chart 15. A portion of this work had been reported in a preliminary communication.\(^{13}\)

A fully functionalized tetracyclic gibberellin intermediate 371 was synthesized via a route shown in Chart 16.\(^{14}\)

A-ring functionalization of hydrofluorene compound 372 derived from abietic acid was accomplished by hypoiodite reaction, as shown in Chart 17.\(^{15}\)
For the synthesis of the gibberellin skeleton, the four possible stereoisomers 374, 375, 376, and 377 and their esters were prepared[176] from 373 which had been synthesized from abietic acid.

Furthermore, nitration of diesters of above four compounds gave only 13-nitro compounds, and, in contrast, its dehydro-derivative 378 was nitrated to give only 12-nitro compound 379.[177]

Syntheses of 12- and 13-hydroxy diesters (380, 381, 382, and 383) regarded as important intermediates for the formation for D-ring in gibberellin, were accomplished in the trans (384) and cis-A/B-ring fused isomer (385) by reduction in lithium–liq. ammonia system and then by hydration with mercuric acetate. The 12-hydroxy diester 386 obtained by epimerization at C-6 of the unstable form 380 has the same skeleton as in A- and B-rings of gibberellin A_{12}.[178]
The sequence of oxidation on ring B in kaurene-gibberellin biosynthesis was investigated. The results of incubation of \([6\beta\text{-}^3\text{H},17\text{-}^{13}\text{C}]-\text{ent-7a-hydroxy-16-kauren-19-oic acid}\) showed that 6\(\beta\)-hydrogen atom is lost in the formation of gibberellic acid. However, \(\text{ent-6a,7a-dihydroxy-16-kauren-19-oic acid (387)}\) was not incorporated into gibberellic acid. Experiments with \([1\text{-}^3\text{H},1\text{-}^{13}\text{C}]\)-geranyl pyrophosphate suggested that the 6\(\beta\)-hydrogen atom migrates to C-7 during ring contraction.\(^{19}\)

A significant specific incorporation of \([^{14}\text{C}]-\text{gibberellin A}_{13}\) anhydride (388), which was prepared from 7\(\beta\)-hydroxy-kaurenoic acid as shown in Chart 18, into gibberellin \(\Lambda_4/\Lambda_7\) fraction (0.07\%\) was recognized. However, there was no detectable incorporation into these substances from the \([^{14}\text{C}]-\text{gibberellin A}_{13}\) (389).\(^{190}\)

**Chart 18**

Fluorogibberellic acid 390 and fluorogibberellin \(\Lambda_9\) 391 were produced by a fermentation of \(G. fujikuroi\) to which \(\text{ent-4a-fluoromethyl-16-gibberellen-7-al-19-oic acid (392)}\) had been added.\(^{181}\)

It had previously been reported that \(\text{ent-kaura-2,16-dien-19-ol (393)}\) is converted to gibberellane derivative 394 by \(Gibberella fujikuroi\). Examination of the less polar methyl esters of the acidic metabolites derived from 393 or its hemisuccinate ester 395 gave four gibberellane derivatives, 396, 397, 398, and 399.\(^{182}\)
Tritium labeled gibberellin A₄ (400) synthesized from GA₃ was imbibed to seeds of Phaseolus vulgaris. Its radioactive metabolic products were [³H]-GA₃-glucoside (401) and [³H]-GA₆ (402). The absence of radioactive GA₃ and GA₃-glucoside was indicated.\(^{183}\)

It was demonstrated that species belonging to two genera of the same family elaborate different antheridiogens. Thus, the structural diversity of antheridiogens may reach the genus level. The question whether such diversity reaches the species level was investigated by comparing the structure of the recently characterized antheridiogen of Anemia phylilitidis with that of A. hirsuta, which showed that both substances are the same and have structure 403.\(^{184}\)

In a review on evolution and biosynthesis of terpenoid pheromons and hormons, gibberellins A₃, A₅, and A₁₅ were described.\(^{185}\) In another review on the principles of promotion and inhibition of growth in plants, gibberellins were described.\(^{186}\)

**XII. ATISANE DERIVATIVES**

A new diterpene, 7α-hydroxy-4-epitrachylobanic acid (404), was isolated from Helianthus ciliaris.\(^{187}\)

The structure of staphisine, a novel diterpene alkaloid dimer isolated by Jacobs and Craig\(^{188}\) in 1941 from the mother liquors accumulated during the isolation of delphinine from the seeds of Delphinium staphisagria, was established by a single-crystal X-ray structure determination of the monomethiodide (405).\(^{189}\)

See also IX, ref. 118.
The mass spectral studies of ajaconine from Delphinium ajacis seeds were carried out. The crystalline sample earlier identified as pure ajaconine was found to be a mixture of five compounds when analysed as their trimethylsilyl derivatives on a mass spectrometer-gas chromatograph. Structures 406 and 407 were assigned to gas-liquid chromatography peak 2 ajaconine and peak 3 ajaconine, respectively.189

A new angular alkylation through intramolecular carbenoid insertion was performed to afford some key intermediates toward diterpene alkaloids and C_{20} gibberellins syntheses. The outline was shown in Chart 19.189

ent-(16R)-Atisan-15-one (408) and small amounts of ent-(16R)-kauran-15-one (409) were yielded by the treatment of ent-kaurane 15β,16β-epoxide (410) with boron trifluoride-ether complex in benzene. In the conversion of 408 into ent-atis-15-ene (411), the 15-tosylates 412 and 413 of the epimeric ent-atisan-15-ols were found to rearrange to the olefin 414 in high yield.189
Atisine (415) had been converted into the epimeric toluene-p-sulfonates 416 and 417. Acetolysis of 416 or 417 afforded the same 14(8→15)abeo-17-oxa-8-ene 418. In contrast, whereas gas phase pyrolysis of 416 gave the olefin 418, the isomer 417 gave a 9(8→15)abeo-17-oxa-8(14)-ene 419.

Each conversion took place stereospecifically via a seven-membered transition state. The structure of olefin 419 was confirmed by an X-ray analysis of the derived ethylene acetal hydriodide (420).193)

XIII. ACONANE DERIVATIVES

Karacoline, a new diterpene alkaloid, was isolated from Aconitum karacolicum, and assigned structure 421.194)
Adsorption chromatography of the mixture of alkaloids obtained from roots of the plant Aconitum ferox yielded four known alkaloids which were identified as pseudaconitine (422), bikhaconitine (423), chasmaconitine (424), and indaconitine (425).¹⁹⁵

\[
\begin{align*}
(421) & \quad R^1=OH, R^2=Ac, R^3=\text{veratroyl}, \\
(422) & \quad R^1=OH, R^2=\text{veratroyl}, \\
(423) & \quad R^1=H, R^2=\text{veratroyl}, \\
(424) & \quad R^1=H, R^2=\text{PhCO} \\
(425) & \quad R^1=OH, R^2=\text{PhCO}
\end{align*}
\]

The structures for A (426) and B (427), two unknown alkaloids of Delphinium bicolor, and the utility of the carbon-13 magnetic resonance technique to the diterpene alkaloids were reported.¹⁹⁶

The mass spectra were examined in order to investigate splitting of ring A substituents of several lycoctonine alkaloids.¹⁹⁷

The optically active delphinine degradation product 429 was stereoselectively synthesized via several steps from methoxy tetralone (428). Thus, it was clarified that the configuration of the ring A methoxyl group in delphinine had to be reversed in comparison with the previously reported structure and this alkaloid had to be represented by the formula 430. The compound 429 or its derivatives constituted an extremely favorable advanced relay for the synthesis of delphinine.¹⁹⁸

The details of an X-ray analysis of the acid oxalate of compound 429 were published, which confirmed the stereochemistry at C-1.¹⁹⁹ This work had been reported in a preliminary communication.²⁰₀
Photochemical behavior of taxinine (431) and its derivatives was investigated. Irradiation on 431 with a 450-W high-pressure Hg lamp in dioxane for 15 min afforded quantitatively a nonseparable 1:1 mixture of transannular products 432 and 433, which upon hydrogenation over Pd/C-AcOEt gave the single dihydro compound 434. Analogously, irradiation on 435 gave the transannular product 436 in quantitative yield.20 On the other hand, irradiation on 437 for 5 hr in dioxane yielded 48% of cyclopropyl ketone 438201,202) and 8% of transannular ketone 436, with recovery of 38% of the starting material.

Irradiation on 439 in t-BuOH for 10 hr gave, after the separation, 65% of the isomeric cyclopropyl ketone 440 and 32% of the solvent adduct 441.201)

XV. THE OTHERS*

It was established by chemical and spectroscopic evidence, and an X-ray analysis of the bis-acetonide that aphidicolin, an antibiotic produced by Cephalosporium

* See also VI, ref. 79.
aphidicola, was shown to contain a novel tetracyclic diterpenoid ring system and to have structure 442.\(^{203}\)

Besides fusicoccin (443), a highly phytotoxic compound, culture filtrates of Fusicoccum amygdali contain a number of by-products. Four of them were also produced when fusicoccin was incubated. They might be derived non-enzymically from fusicoccin in the process of the fermentation. The structures of two of these compounds, monodeacetylfusicoccin (444) and dideacetyl-fusicoccin (445), had been established. The other two products, allofusicoccin and isofusicoccin were characterized and assigned structures 446 and 447, respectively.\(^{204}\)

Three isomers of monodeacetylfusicoccin, monodeacetylarfusicoccin (448), monodeacetyliso-fusicoccin (449) and 12-O-acetyl-dideacetyl-fusicoccin (450) were also isolated from the culture filtrates of F. amygdali as minor co-metabolites.\(^{205}\)

From the benzene extract of Sapium japonicum twigs and bark, a piscicidal diterpene was isolated. Its structure was determined as 451 on the basis of its UV, IR, PMR, and mass spectra and those of its derivatives. The piscicidal activity of this substance is 4 times that of rotenone.\(^{206-207}\)
Bromination reactions of phorbol pentaacetate (452) were investigated. Four types of brominations, after column chromatographic separations, afforded 453, 454, and 455. The compounds, 453 and 455, might be formed by intramolecular acetyl migration ($\text{C}_9\text{-OAc} \rightarrow \text{C}_7$) of each primary labile $\text{C}_7\beta$-bromo product during chromatographic purification.208)

The structure elucidation of cotylenol (456), a new metabolite produced by a fungus strain 501-7W, was published. Cotylenol was found to be the aglycone of the leaf growth substances cotylenins A and B.209)

\[
\begin{align*}
\text{(456)} & \quad \text{(457a)} \quad \text{(457b)} \\
\text{(459)} & \quad \text{(458a)} \quad \text{(458b)}
\end{align*}
\]

The structures of cyathin A$_3$ and allocyathin B$_3$, metabolites of the bird's nest fungus *Cyathus belenae*, were reported. The former was shown to have the equilibrium structure between 457a and 457b in the solution, and the latter was assigned structure 458. Single crystal of cyathin A$_3$ was, however, established to have structure 457b by the X-ray analysis. Its relative configuration 459 was also clarified.210

Cyathin A$_3$ and allocyathin B$_3$ are new diterpenes having novel carbon skeleton.

Some diterpenes, strobol (460), strobal (461), manoyl oxide, and cis- and trans-abiens, were isolated as major constituents of the extract of *Pinus strobus* cortex tissue.211)

\[
\begin{align*}
\text{(460)} & \quad \text{(461)} \\
\text{(462)} & \quad \text{(463)}
\end{align*}
\]

A new macrocyclic diterpene, isoincesole-oxide (462), was isolated from Frankincense in very small amount. The structure was deduced on the basis of the chemical and physicochemical data.212

Neocembrene A, a trail pheromone of Nasutitermes, was shown to be the cembrene analogue 12-isopropyl-1,5,9-trimethylcyclotetradeca-1,5,9-triene (463) by degradation, by comparison of its perhydro-derivative with perhydrocembrene, and by
isomerization with sodium methylsulfinylmethanide followed by degradation. The configurations of the double bonds are unknown.213

The monocyclic diterpenes, α-camphorene (464), cembrene (465), and allylcembrol (466) were isolated from gum resin of Commiphora mukul.214

\[
\text{HO} \quad (464) \quad (465) \quad (466)
\]

The crystal structure of all-trans retinal was determined by an X-ray analysis as 467.215

An X-ray analysis of 11-cis-retinal (468) was independently executed, and reported.216 The details of geometry of all-trans and 11-cis retinals are considerably interested in explanation of the photoreceptor process.

\[
\text{(467)} \quad \text{(468)}
\]

4-Oxoretinoic acid (469) was prepared from methyl retinoate by oxidation with MnO₂ and hydrolysis of the resulting keto ester 470. Sodium borohydride reduction of 469 or 470, followed by dehydration and hydrolysis afforded vitamin A₂ acid. Compounds 469 and 470 showed lower vitamin A activity than retinoic acid in rats.217

It was clarified that the bacteriochlorophylls isolated from Chromatium vinosum and Rhodopseudomonas spheroides are esters of phytol and the bacteriochlorophyll isolated from Rhodospirillum rubrum (Athiorhodaceae) is esterified at the propionic acid side chain by all-trans-geranylgeraniol (471).218

The terpenoid antibiotic LL-Z 1271a (473) was synthesized from the (+)-ketolactone 472 obtained by degradation of marrubiin. The synthetic route is shown in Chart 20.219

\[
\text{(469) } R=\text{H} \\
\text{(470) } R=\text{Me}
\]

\[
\text{(471)}
\]
A comparison of the NMR and mass spectra of bilobalide $\text{C}_{15}\text{H}_{18}\text{O}_8$ and of the ginkgolides $\text{C}_{20}\text{H}_{24}\text{O}_9$–11 was described.\textsuperscript{220}

Three reviews "the structures and syntheses of natural products" were published in Japanese, in which pimarane type and tetracyclic diterpenes were described.\textsuperscript{221,222,223}

In a Japanese review on the rooting promotor and rooting inhibitor, portulac isolated from Portulaca grandiflora, was described.\textsuperscript{224}

A brief list of the references on plant physiological substances was published, in which the references of gibberellin $A_{37}$ and $A_{38}$ glucosyl ester were shown.\textsuperscript{225} In a Japanese review "active constituents of piscicidal plants", callicarpone, maingayic acid, huratoxin, and some other diterpenes were described.\textsuperscript{226}

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