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The Chemistry on Diterpenoids in 1968

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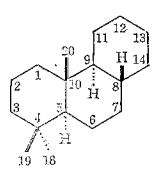
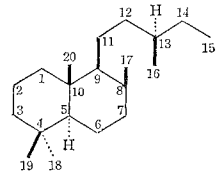
I. INTRODUCTION

The author has published a series of the reviews.[1~4] This review deals with an outline of the chemical works on diterpenoids in 1968.

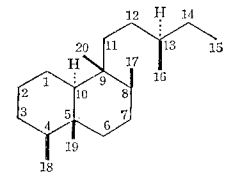
The classification consists of podocarpane, labdane, clerodane, pimarane, isopimarane, abietane, totarane, cassane, kaurane, gibberellane, atisane, aconane, beyerane, taxane, and the others, in accordance with a poposal** for systematic nomenclature subscribed to by most workers in this area.[5]



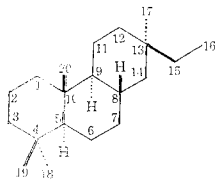
Podocarpane



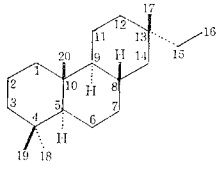
Labdane



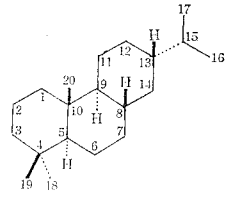
Clerodane



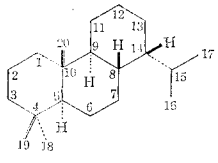
Pimarane



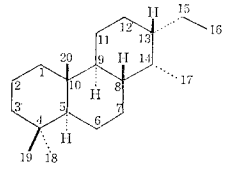
Isopimarane



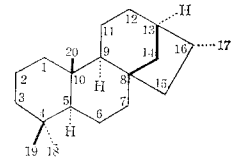
Abietane



Totarane



Cassane



Kaurane

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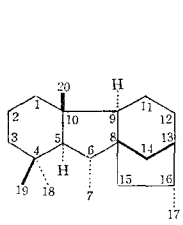
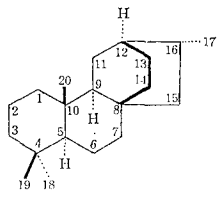
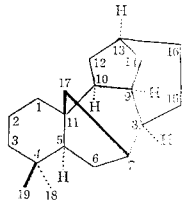
** The IUPAC Commission on the Nomenclature of Organic Chemistry has discussed these proposals and considered that they are as a whole in accordance with the general principles of the nomenclature of organic chemistry.



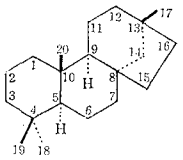
Gibberellane



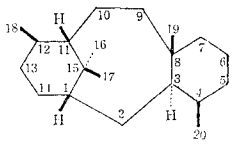
Atisane



Aconane



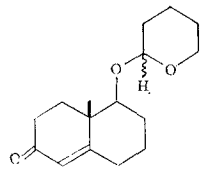
Beyerane



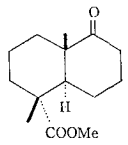
Taxane

II. PODOCARPANE DERIVATIVES

Methyl *rac*-deisopropyldehydroabietate (3)*[3] was derived from 1*[3] *via* 2*[3] by Spencer *et al.*[6] The synthesis was developed to that of podocarpic acid, that is,



(1)



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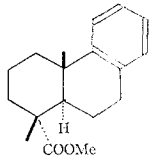
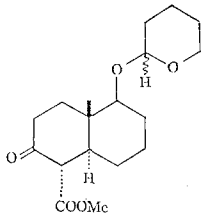


(3)

methyl *rac*-podocarpate (6)*[3] was synthesized[7] from 4*[3] *via* 5.*[3] Methyl 12-methoxypodocarpa-8, 11, 13-trien-19-oate (7) was converted into 8. The corresponding acid chloride 9 was subjected to Friedel-Crafts cyclization to yield D-



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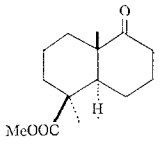

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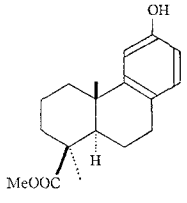

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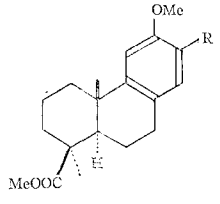
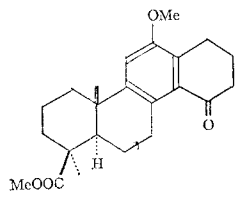


(7) : R=H
(8) : R=$(CH_2)_3COOH$
(9) : R=$(CH_2)_3COCl$

homosteroid **10**. Lactone **11** was formed by Reformatsky reaction of 13-succinyl derivative. The rearrangement of C-12 O-allyl ether gave normal C-13 allyl

*[3] Represented as one enantiomer.



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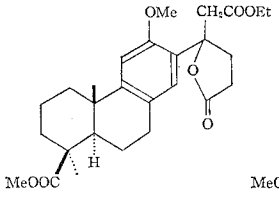

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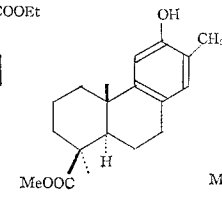

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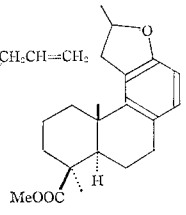
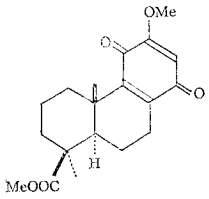


(13)

phenol **12** and coumaran **13**. Peracid oxidation of **7** gave the expected quinone **14** and hydroxy dienone **15**. Unsaturated ketone **16** on photolysis in methanol gave only the corresponding saturated ketone **17**.[8]



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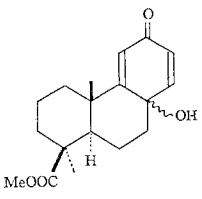

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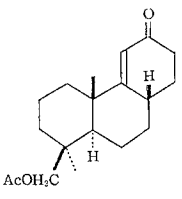

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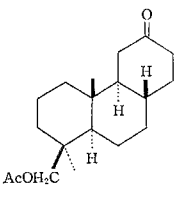
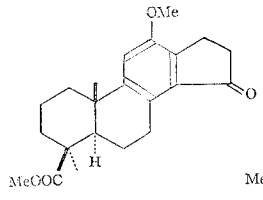


(17)

Compound **18** was prepared from **19** in a fair yield, but attempted cyclization of compounds possessing a 1′-substituted-2′-carboxyethyl side chain at C-13 was unsuccessful. The C-17 ketone **20** was obtained in low yield from the 13-acrylyl



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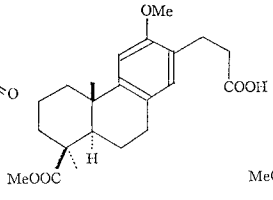

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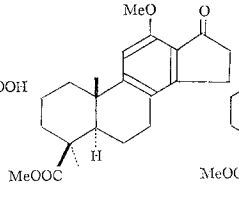

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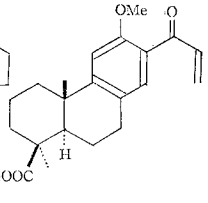
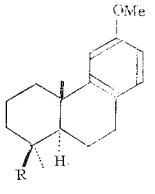
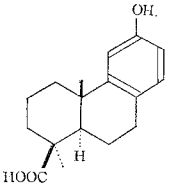


(21)

compound **21**.[9] The conversion of O-methylpodocarpic acid (22) into 12-methoxy-19-norpodocarpa-8, 11, 13-trien-4-amine (23) was investigated.[10] A variety



(22) : R=COOH
(23) : R=NH_2



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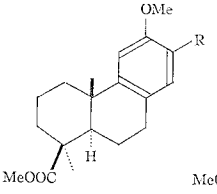
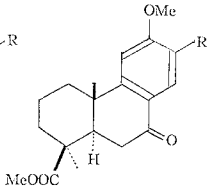


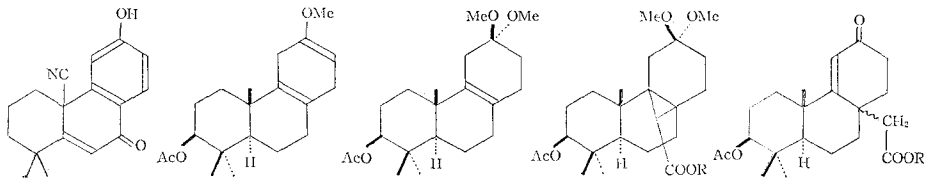
(25) : R=H
(26) : R=Br
(27) : R=Et
(28) : R=^nPr
(29) : R=COMe
(30) : R=COEt



(31) : R=H
(32) : R=Br
(33) : R=Et
(34) : R=^nPr
(35) : R=COMe
(36) : R=COEt

of derivatives of podocarpic acid (**24**), for instance, **25**~**30**, gave their corresponding 7-oxo-compounds, **31**~**36** in moderate to good yield by a brief treatment with bromine in ether, preferably containing a free-radical initiator such as benzoyl peroxide, followed by hydrolysis.[11]

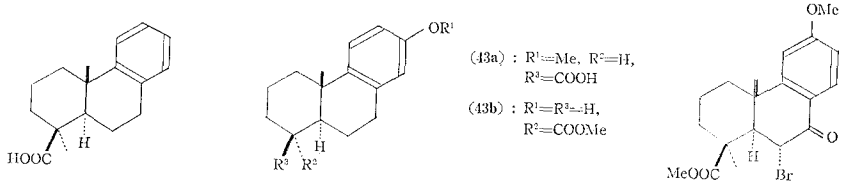
10-Cyano-12-hydroxy-7-oxo-20-norpodocarpa-5, 8, 11, 13-tetraene (**37**), a model for *tricyclic* C-aromatic diterpenoids, was synthesized.[12]



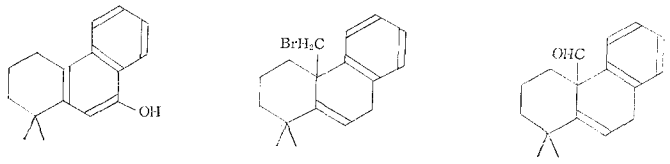
(37) (38) (39) (40) (41)

Stipanovic and Turner[13] attempted to synthesize **41** from **38** *via* **39** and **40**, but the reaction of diazoacetic ester on **39** was unsuccessful and **40** was not obtained. They examined the same reaction using more simple models.

A stereoselective synthesis of *rac*-desoxypodocarpic acid (as **42**) and *rac*-13-methoxydesoxypodocarpic acid (as **43a**) was reported by Ireland and Giarrusso.[14a] Methyl 13-hydroxydeisopropyldehydroabieatate (**43b**) was synthesized by an Indian group.[14b] The stereochemistry of 6-bromo-7-oxo derivative **44** was established by X-ray analysis. Bromination of sugiyl methyl ether was examined.[15] Conformational analysis of 6-bromo-7-oxopodocarpic acid derivatives was tried by application of the Nuclear Overhauser Effect.[16] Okamoto *et al.*[17] published a



(42) (44)



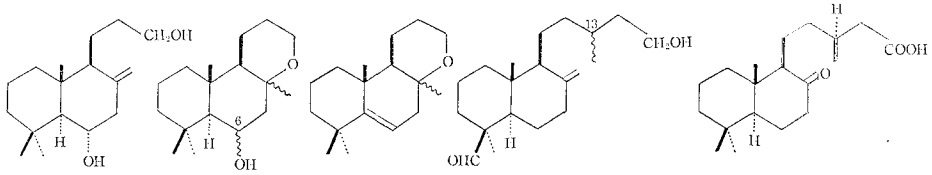
(45) (46) (47)

new method for angular formylation using Reimer-Tiemann's reaction. They prepared **47** *via* **46** starting from **45**.

III. LABDANE DERIVATIVES

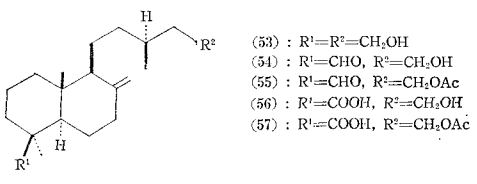
14, 15, 16-Trisnor-labd-8(17)-ene-6α, 13-diol (**48**) was subjected to cyclization

in the presence of p-toluenesulfonic acid to give 6α- and 6β-hydroxy-8, 13-oxido-14, 15, 16-trisnorlabdane (**49a, b**), which were dehydrated to yield a same unsaturated product **50**.[18] 19-Oxo-labd-8(17)-en-15-ol (**51**) (imbricatolal), from the

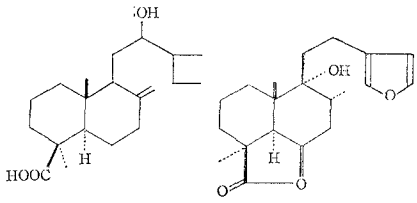


(18) (49a) : 6α OH (49b) : 6β OH (50) (51) (52)

oleoresin of *Araucaria imbricata*, was converted into 17-nor-8-oxy-labdan-15-oic acid (**52**) by Bruns.[19] Thus, the S-configuration at C-13 in imbricatadiol (**53**), imbricatolal (**51**=**54**), imbricatolal-15-acetate (**55**), imbricatolic acid (**56**), and imbricatolic acid-15-acetate (**57**) was proved.

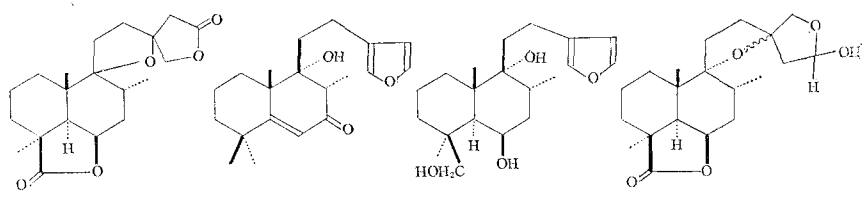


(53) : R^1=R^2=CH_2OH
(54) : R^1=CHO, R^2=CH_2OH
(55) : R^1=CHO, R^2=CH_2OAc
(56) : R^1=COOH, R^2=CH_2OH
(57) : R^1=COOH, R^2=CH_2OAc



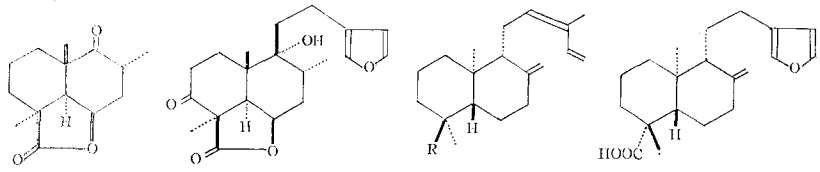
(58) (59)

From *Juniperus phoenicea*, 12-hydroxylabd-8(17)-en-19-oic acid (**58**) was isolated.[20] Mangoni and Adinolfi[21,22] established the stereochemistry of marrubiin, especially that of C-9 hydroxy group, as shown in formula **59**. The structures of compounds X and Y, two labdane diterpenoids isolated together with marrubiin from *Leonotis leonurus*, were elucidated as shown in formulas **60** and **61**, respectively.[23] In the absence of pyridine dehydration of marrubiin with phosphorus trichloride appears to yield exclusively the $\Delta^{9(11)}$-olefin whereas in its presence the Δ^8-isomer predominates.[24] From *Marrubium vulgare*, marrubenol (**62**) and the hemiacetal **63** were isolated besides marrubiin.[24] A partial synthesis



(60) (61) (62) (63)

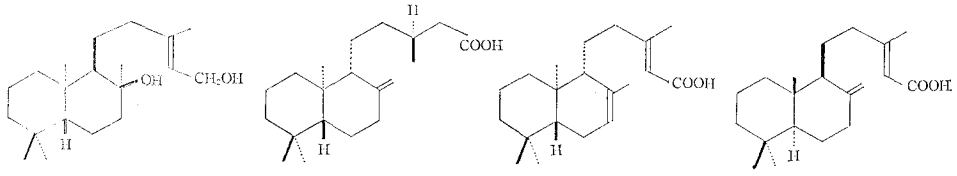
of marrubiin from compound **64** was carried out.[25] From *Marrubium incanum* a new diterpenoid **65**,[26] whose physical properties correspond with those described by L. A. Salei *et al.*,[27] was isolated. A full paper on the structure **66** of ozic



(64) (65) (66) : R=COOH (67) : R=CH_2OH (68)

acid isolated from the wood of *Daniellia ogea* was published.[28] The corresponding alcohol, ozol (**67**) was also isolated. From the wood of *D. oliveri* daniellic acid (**68**) was isolated. Chromic acid oxidation of sclareol was investigated and isolation of at least seven compounds was effected by chromatography of the methylated products. No pimarane derivatives were obtained.[29]

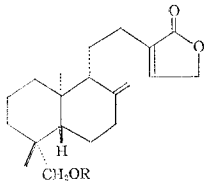
From oleoresin of black kauri *cis*- (**69**) and *trans*-communic acid (**70**), abietic acid, neoabietic acid, agathic acid (**71**), methyl agathate, and a new aldehydic carboxylic acid, agathalic acid (**72**) were isolated. The latter was reduced to agatholic acid (**73**) by sodium borohydride.[30] From the dry leaves of *Aphanamixis polystachya* aphanamixol (**74**) was isolated.[31] Eperuic acid (**75**), its Δ^7-isomer, *ent*-7, 13-labdadien-15-oic acid (**76**), 8(17), 13-labdadien-15-oic acid (**77**), and the enantiomer (named "copalic acid") of **77** were isolated from *Oxystigma oxyphyllum*.[32]



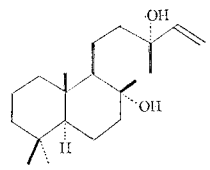
(69) (70) (71) (72) : R=CHO (73) : R=CH_2OH

(74) (75) (76) (77)

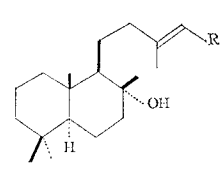
The structure **78** was proposed for neoandrographolide, a diterpene glucoside from *Andrographis paniculata*.[33] Dehydration investigation of sclarealdehyde (**80**), a product from chromic acid oxidation of sclareol (**79**) was reported.[34] The chromic acid oxidation product of sclareol, which was a mixture containing sclarealdehyde (**80**), was subjected to lithium aluminum hydride or sodium borohydride reduction. From the reaction mixture, diol **81** was isolated as acetate.[35] Two new isoambreinolides, **82** and its 8-epimer **83**, were synthesized and characteriz-



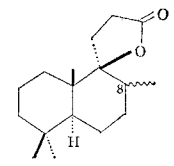
(78) : R=glucose



(79)

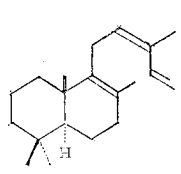


(80) : R=CHO
(81) : R=CH_2OH

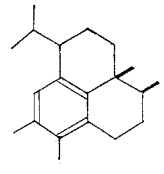


(82) : 8α-Me
(83) : 8β-Me

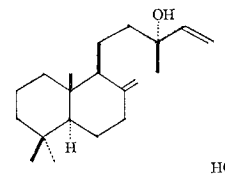
ed.[36] Ruzicka and Janot[37] treated sclareol (**79**) with β-naphthalenesulfonic acid at 190° and got a hydrocarbon $C_{20}H_{32}$, to which they assigned structure **84**. Carman and Dennis[38] reinvestigated the reaction and got a hydrocarbon $C_{20}H_{30}$, to which they assigned structure **85**. They provided a rearrangement mechanism for the product formation. Manool (**86**) and agathadiol (**87**) cyclize in formic



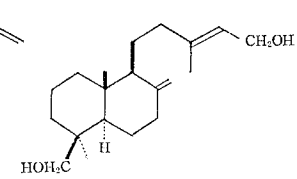
(84)



(85)

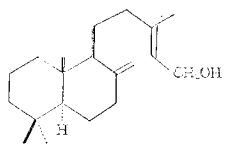


(86)

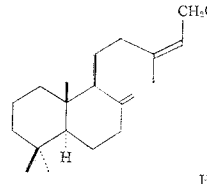


(87)

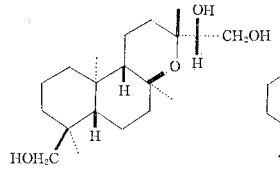
acid to the 13-epimeric pimara-8, 15-dienes and 14α-hydroxybeyerane derivatives. The mechanistic and biosynthetic implications of these results and the nuclear magnetic resonance spectra of relevant tricyclic and tetracyclic diterpenes were discussed.[39] Manool (**86**), 13-epimanool, and the allylic primary alcohols **88a** and **88b** were subjected to acid-promoted dehydration [AcOH-H_2O-H_2SO_4 (83 : 10 : 7) at



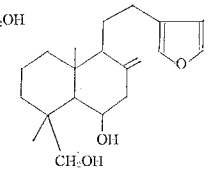
(88a)



(88b)



(89)

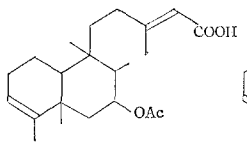


(90)

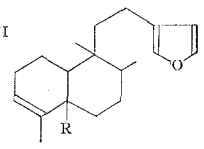
50°]. The four labdadienols gave product mixtures of essentially similar composition which varies with time. Their *in vitro* conversion into pimara- and rosa-dienes was discussed.[40] A new diterpene triol was isolated from *Goodenia ramelii*, and structure **89** was assigned to it.[41] Extracts of the leaves of *Psiadia altissima* contained diterpenoid glycosides, the major aglylcone of which is probably **90**.[81b]

IV. CLERODANE DERIVATIVES

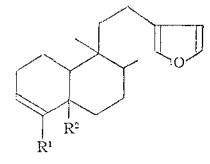
A bitter principle was isolated from the roots of *Solidago altissima* and named solidagonic acid, whose structure **91** was elucidated by Kotake *et al.*[42] From



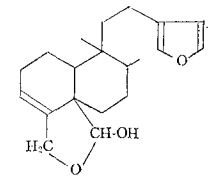
(91)



(92a) : R=COOH
(92b) : R=CHO

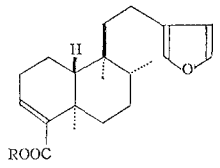


(93) : R^1=CH_2O-angeloyl, R^2=COOH
(94) : R^1=R^2=CH_2OH
(95) : R^1=R^2=CHO

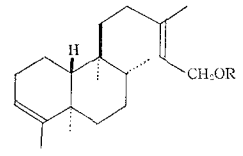


(96)

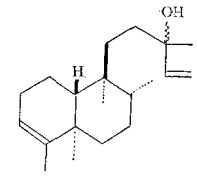
the roots of *Solidago serotina* furan-containing clerodane derivatives were isolated and structures **92** to **96** were tentatively assigned to them.[43] The absolute configuration **97** was assigned to (−)-hardwickiic acid.[44a] Kolavelool (**101**) and methyl hardwickiate (**98**) were derived from kolavenol (**99**) and its acetate (**100**), respectively.[44b] Constitution and configuration of diosbulbin -A, -B, and -C were elucidated as **102**, **103** and **104** by chemical and physical methods. They were



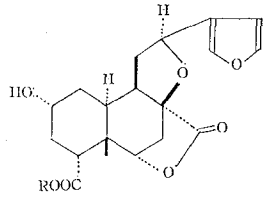
(97) : R=H
(98) : R=Me



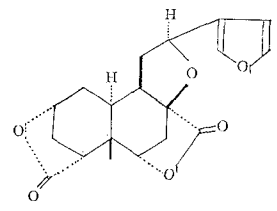
(99) : R=H
(100) : R=Ac



(101)



(102) : R=Me
(104) : R=H



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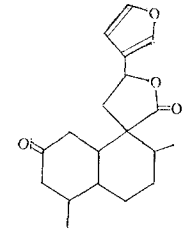
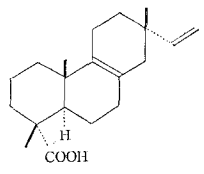


(105)

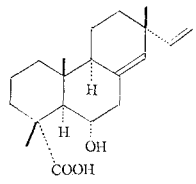
isolated from Dioscoreaceous plants.[45] The full paper of the assignment of structure **105** to crotonin, a norditerpene from *Croton lucidus*, was published.[46]

V. PIMARANE AND ISOPIMARANE DERIVATIVES

8, 15-Isopimaradien-18-oic acid (**106**) was isolated as methyl ester from balsam of *Pinus peuce*.[47] From the acidic fraction of the extract of *Juniperus phoenicea* a new hydroxyacid diterpene was isolated and characterized as 6α-hydroxysandaracopimaric acid (**107**)[48] The structures of virescenol A and B, metabolites of *Oospora virescens*, were elucidated as shown in formulas **108** and **109**, respectively.[49] They readily undergo an acid-catalyzed isomerization to afford isovirescenol A and B, which have $\Delta^{8(9)}$ instead of Δ^{7}. Isolation and constitution of oblongifoliol, a new diterpene of *Croton oblongifolium*, was reported. Its structure was



(106)



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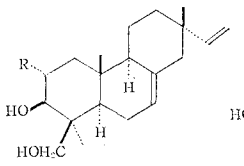
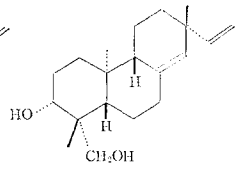
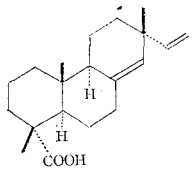


(108) : R=OH
(109) : R=H

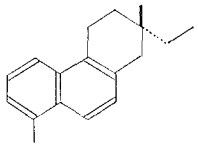


(110)

shown to be *ent*-3β, 19-dihydroxypimara-8(14), 15-diene (**110**).[50] Sandaracopimaric acid (**111**) was synthesized starting from testosterone acetate *via* 14 steps.[51] As catalytic dehydrogenation product of sandaracopimaric acid (**111**), compound **112** had been obtained. Now, this optically active compound was synthesized from R-(−)-methylethylsuccinic acid (mono methyl ester) and 5-methylnaphthylmagnesium bromide.[52] Isolation and structure of a new diterpene lactone from *Trichothecium roseum* was published. The substance was formulated as 6β-hydroxyrosenonolactone (**113**) on the basis of chemical and spectroscopic evidence.



(111)



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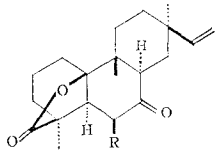
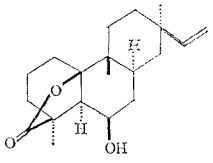
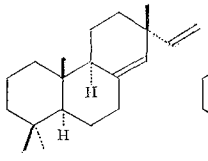


(113) : R=OH
(114) : R=H

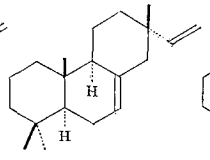


(115)

Circular dichroism data on lactones possessing the same skeleton were discussed.[53] Biosynthesis of rosenonolactone was studied. Geranylgeraniol was incorporated in rosenonolactone (**114**). In the course of biosynthesis the hydride shift from C-9 to C-8 should be involved. This proposal was proved to be correct by feeding of doubly-labelled 4R-[4[3]H: 2-[14]C] mevalonic acid lactone. Deoxorosenonolactone was incorporated into rosenonolactone (**114**) and rosololactone (**115**).[54]



(116)



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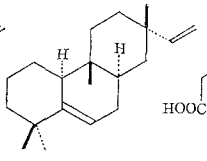

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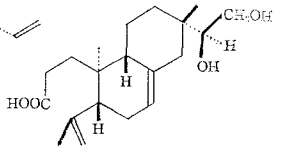


(119)

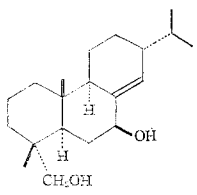
Manool (**86**) was treated with formic acid in chloroform to give three pimarane and isopimarane derivatives and a beyerane derivative. From the products sandaracopimaradiene (**116**), isopimaradiene (**117**), and rimuene (**118**) were derived chemically.[55] The similar experiments on cyclization of manool were reported.[39,40]

A new acid was isolated from *Beyeria brevifolia*, and its structure was eluci-

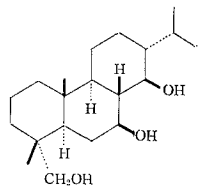
dated as shown in **119**.[56]

VI. ABIETANE AND TOTARANE DERIVATIVES

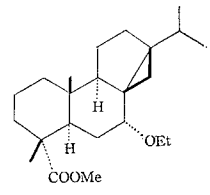
Monohydroboration-oxidation of abietic acid and methyl abietate with both diborane and *t*-2, 3-dimethylbutylborane led to preferential attack on the 7, 8-double bond to give 7-hydroxy-8(14)-enes, *e.g.*, **120**. Dihydroboration-oxidation with these reagents yielded mainly 7β, 14β-dihydroxy derivatives, *e.g.*, **121**, with smaller



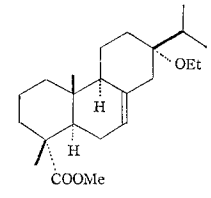
(120)



(121)

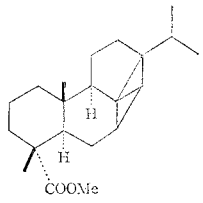


(122a)

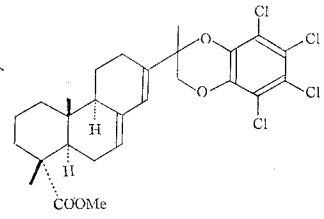


(122b)

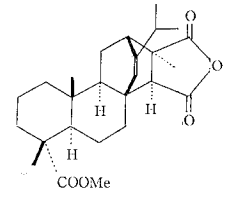
amounts of the 7α, 14α-dihydroxy-compounds and a third 7, 14-diol of unknown stereochemistry.[57] Abietic acid in absolute ethanol was irradiated for 96 hours with 2537Å light in the absence of oxygen and then esterfied with diazomethane. Chromatography of the crude product on silica gel gave **122a** and **122b**. The formation of **122a** involves the bicyclobutane intermediate **123**.[58] Treatment of



(123)



(124)



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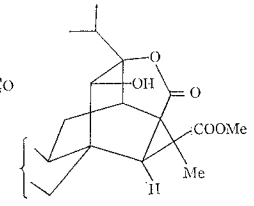
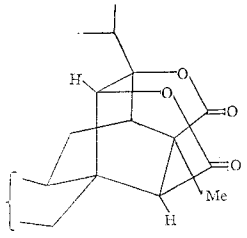
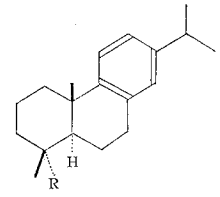


(126)

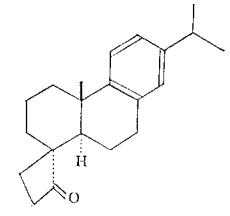
methyl abietate with tetrachloro-*o*-benzoquinone in xylene gave a solid adduct, to which structure **124** was assigned on the basis of spectroscopic investigation.[59] Diels-Alder adducts of citraconic anhydride and methyl resinate were investigated. An adduct **125** was converted into the epoxide, which was subjected to acidic methanolysis to give **126**. The latter was transformed into dilactone **127**.[60] Oxi-



(127)



(128) : R=COOH
(129) : R=COCHN₂
(130) : R=CH₂COOMe
(131) : R=COCH₂OMe

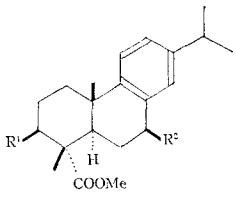


(132)

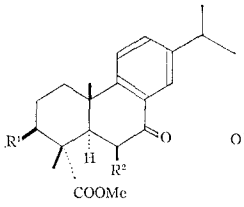
dation of methyl abietate by monoperphthalic acid was investigated.[61] Methyl 12-acetyldehydroabietate was subjected to potassium borohydride reduction to give two kinds of alcohols, which were regarded as rotational isomers between two large substituents at C-11 and C-12. Similarly, lithium aluminum hydride reduction of the same material yielded two kinds of diols.[62]

Treatment of the diazomethyl ketone **129**, derived from dehydroabietic acid (**128**), with a suspension of silver oxide in methanol afforded methyl homodehydroabietate (**130**) (55 %), a liquid ketone **131** (20 %), and a ketone **132** (22 %).[63] Methyl 12-ω-bromoacetyldehydroabietate was heated with thiourea in EtOH to yield methyl 12-(2-amino-5-thiazolyl)-dehydroabietate. Methyl 12-(α-bromopropionyl)-dehydroabietate was treated with thiourea to afford methyl 12-(2-amino-4-methyl-5-thiazolyl)-dehydroabietate.[64]

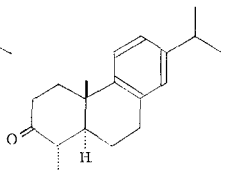
Incubation of methyl dehydroabietate (methyl ester of **128**) with *Corticium sasakii* yielded methyl 3β-hydroxydehydroabietate (**133**) and methyl 3β, 7β-dihydroxydehydroabietate (**134**). Both of 3β-hydroxy **133** and 7β-hydroxy-derivative **135** on incubation with *C. sasakii* gave diol **134**. Incubation of methyl 7-oxode-



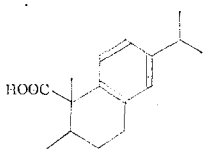
(133) : R^1=OH, R^2=H
(134) : R^1=R^2=OH
(135) : R^1=H, R^2=OH



(136) : R^1=R^2=H
(137) : R^1=OH, R^2=H
(138) : R^1=R^2=OH



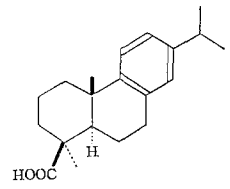
(139)



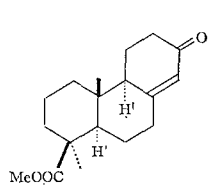
(140)

hydroabietate (**136**) afforded methyl 3β, 6β-dihydroxy-7-oxodehydroabietate (**138**) *via* 3β-intermediate **137**. Hydroxylation appears to occurr first in the C-3 β position, then in the C-6 β or C-7 β position of the dehydroabietanes. Oxygenation of dehydroabietanes at C-3, C-6, or C-7 by this fungal oxidase is analogous to the position of oxygenation of dehydroabietanes obtained from *Juniperus* trees.[65] Degradation of dehydroabietic acid by bacteria (*Flavobacterium resinovorus*) to 3-oxo-19-nor-dehydroabietane (**139**) and the proposed pathway were reported.[66] Methyl dehydroabietate was subjected to microbial degradation by *Arthrobacter sp.* isolated from lodgepole pine to give dehydroabietic acid, methyl 3-oxodehydroabietate, and compound **140** (as methyl ester).[67]

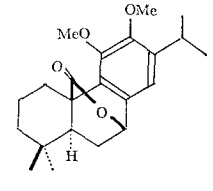
An investigation on the resins of several *Callitris* species (Cupressaceae) led



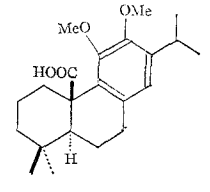
(141)



(142)



(143)



(144)

to isolation of callitrisic acid (**141**), a new diterpenoid.[68] The *rac*-callitrisic acid was synthesized from an intermediate **142**.[69a,b] *rac*-Carnosol dimethyl ether (as **143**) and *rac*-carnosic acid dimethyl ether (as **144**) were synthesized.[70] β-Keto-sulfoxide was effectively used for condensation in the synthesis as shown in Chart 1.

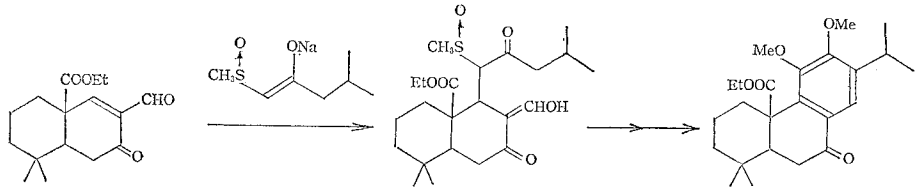
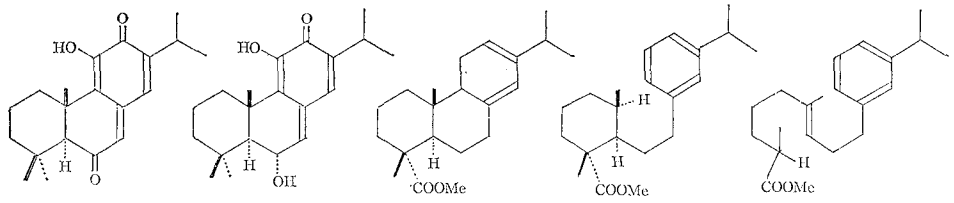


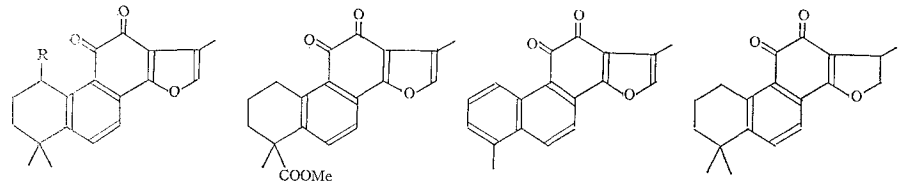
Chart 1

Two novel diterpenoid quinone methides, taxodione (**145**) and taxodone (**146**), were isolated from *Taxodium distichum*. Each showed significant inhibitory activity against the Walker carcinosarcoma 256 in rats, at 40 and 25 mg/kg, respectively.[71] Novel ring openings in methyl levopimarate (**147**) were investigated at 200° in the presence of catalytic amount of KOH. The products were found to be 148, **149**, and *cis* isomer of **149**.[72] From dried red roots of *Salvia miltior-*



(145) (146) (147) (148) (149)

rhiza, two novel pigments, hydroxytanshinone (**150**) and methyl tanshinonate (**151**) were isolated.[73] Total syntheses of tanshinone-I (**152**), -II (**153**), and cryptotanshinone (**154**) were published by two groups.[74a,b] Another short-step syn-



(150) : R=OH
(153) : R=H

(151) (152) (154)

theses were also reported.[75] A stereoselective formation of a tricyclic system and the total synthesis of *rac*-fichtelite (as **155**) was reported by Johnson *et al.*[76] The outline is shown in Chart 2.

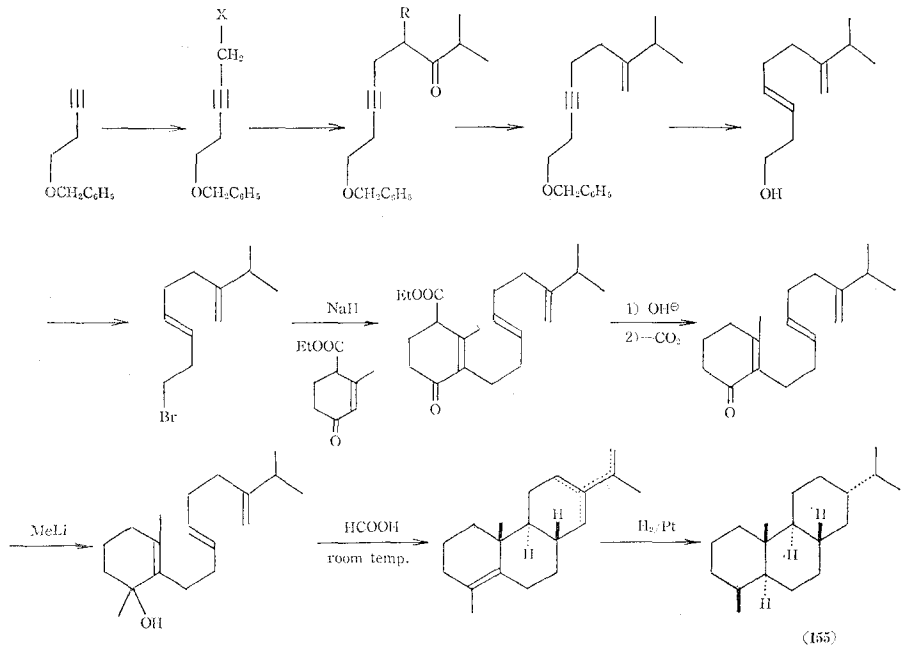
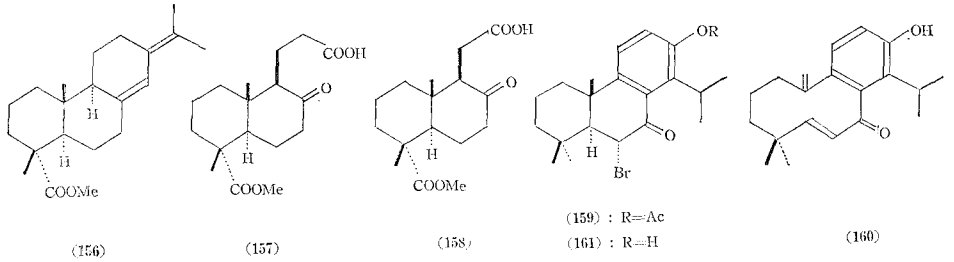
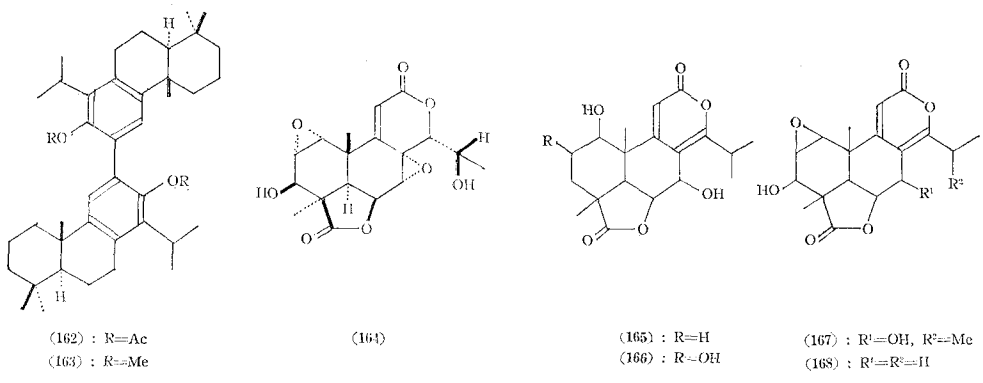


Chart 2

Deamination of 18-nor-4-amino-abieta-8, 11, 13-triene was investigated.[77] Oxidative degradation of methyl neoabietate (**156**) and methyl levopimarate (**147**) yielded **157** and **158**, respectively, both of which can be used as good intermediates for synthesis of diterpenoids.[78]

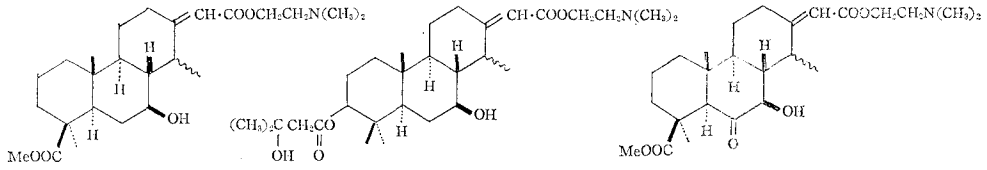




6α-Bromo-7-oxototaryl acetate (**159**) was treated with $NaHCO_3$ in DMSO to give α, β-unsaturated ketones (Δ^5) (60 %) and a secoditerpenoid **160** (5 %). The high yield (80 %) of **160** was achieved when 6α-bromo-7-oxototarol (**161**) was used.[79] A nuclear magnetic resonance study of hindered rotation in biphenyls was carried out using podototarin diacetate (162) and podototarin dimethyl ether (**163**).[80] The structure **164** was assigned to inumakilactone A, a bitter bisnorditerpenoid, isolated from the wood of *Podocarpus macrophyllus*.[81] Structures of nagilactone, A (**165**), B (**166**), C (**167**), and D (**168**), novel nor- and bisnor diterpenoids isolated from *Podocarpus Nagi*, were elucidated.[82]

VII. CASSANE DERIVATIVES

Three new alkaloids were isolated from the bark of *Erythrophleum guineense syn. E. suaveolens*. Chemical and spectroscopic data provided evidence for the structure of two of them, cassamidine (**169**) and coumidine (**170**), and strongly

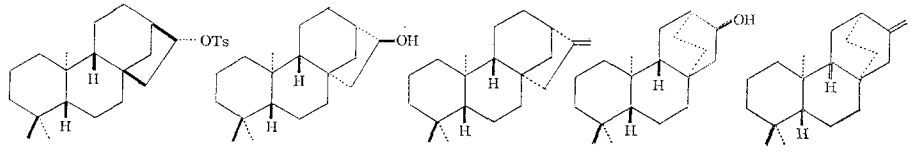


(169) (170) (171)

suggested that the third alkaloid, erythrosuamine is represented by **171**.[83] From the seeds of *Caesalpinia bonducella*, α-, β-, and γ-caesalpin were isolated.[84]

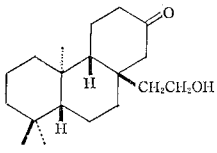
VIII. KAURANE AND BEYERANE DERIVATIVES

Foliage from *Cryptomeria japonica* was analyzed for diterpenoid hydrocarbons by Overton *et al.*[85] Samples grown from some seed sources furnished *ent*-kaurene ((−)-kaurene) as the sole product of this type, whilst those from other sources yielded only phyllocladene. These observations were found to be seasonally independent and it was concluded that *C. japonica* exists in two chemically distinct forms. Combined gas chromatography-mass spectrometry was effectively applied to quantitative analysis of mixtures of diterpene-hydrocarbons.[86] *ent*-17-Nor-16β-tosyloxykaurane (**172**) was heated at reflux with HOAc in the presence of NaOAc to give a mixture of acetates (ca. 90 % yield), from which, after treatment with $LiAlH_4$ alcohol **173** was isolated in 5 % yield. The latter was convert-



(172) (173) (174) (175) (176)

ed into *ent*-phyllocladene (**174**) *via* oxidation followed by Wittig reaction. Similarly, alcohol **175** was isolated from the above mixture in 25 % yield. The same treatment of the alcohol yielded atisirene (**176**). *ent*-17-Noratisan-13-one (**178**) was prepared from *ent*-kaurene *via* the ketol (**177**). Neoatisirene (**179**) was derived from **178** by Wittig reaction.[87] Structures were established for three new diter-



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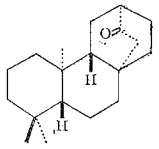

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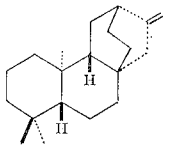
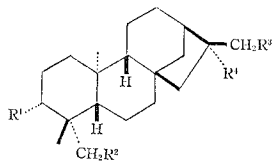
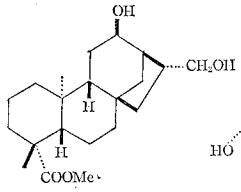


(179)



(180) : $R^1=R^2=R^3=R^4=OH$
(181) : $R^1=R^2=R^4=OH$, $R^3=H$
(182) : $R^1=R^3=R^4=OH$, $R^2=H$

penes, *ent*-kaurane-3β, 16, 17, 19-tetraol (**180**), *ent*-kaurane-3β, 16, 19-triol (**181**) and *ent*-kaurane-3β, 16, 17-triol (**182**), which were obtained from *Beyeria latifolia*.[88] *ent*-12α, 17-Dihydroxy-16β-kauran-19-oic acid was isolated as methyl ester **183** from *Beyeria leschenaultii*. Four known kauranes were also isolated.[89] Isolated of the known kauranes and beyeranes from *Beyeria brevifolia* was reported.[55] A succinate **184** was isolated from *Goodenia strophiolata* accompanied by the known



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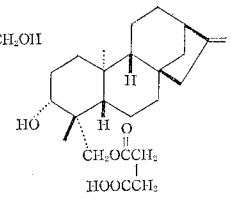

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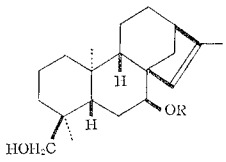
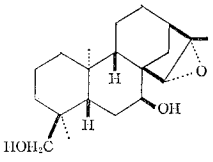
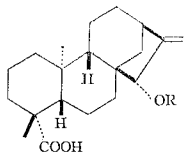


(185) : R=H
(186) : R=Ac

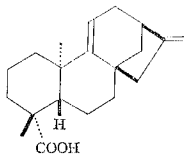


(187)

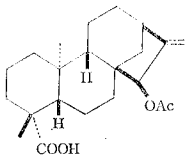
diol.[90] The same diterpenoid was also isolated from *G. ramelii*.[41] From *corols* of *Sideritis sicula*, two new diterpenes, sideridiol and siderol were isolated. Structures **185** and **186** were assigned to them. The absolute configuration was established by correlation with *ent*-isokaurene.[91] Further investigation led to isolation of third diterpene, sideroxol, whose structure was elucidated as shown in formula **187**.[92] On the basis of chemical and spectroscopic evidence, structure **188** was assigned to grandiflorolic acid extracted from the resin of *Espeletia grandiflora*.[93] Similar diterpenoids **189** and **190** were isolated together with **188**



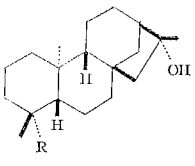
(188) : R=H
(189) : R=Ac



(190)

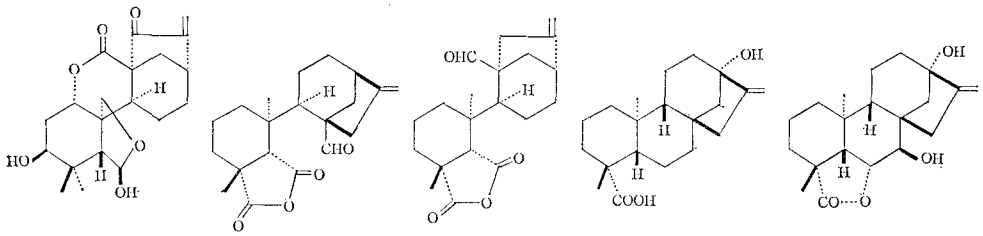


(191)



(192) : R=CHO
(193) : R=COOH

from *E. schultzii*.[94] The structure **191** was assigned to xylopic acid, a new diterpenic acid isolated from *Xylopia aethiopica*.[95] *ent*-16β-Hydroxykauran-19-al (**192**) and *ent*-16β-hydroxykauran-19-oic acid (**193**) were isolated among other metabolites from a large-scale fermentation of *Fusarium moniliforme*.[96] Recently the bitter principles of the *Isodon* species have been shown to be kauranoid diterpenes. Induced amongst these are a number of compounds of which enmein (**194**) is the best known, where ring B of the kaurene skeleton has been cleaved. Fujenal (**195**) from *Gibberella fujikuroi* represents another example of this series. Cleav-



(194) (195) (196) (197) (198)

age between C-6 and C-7 permits rotation about the 9-10 bond. Molecular models suggest that this rotation is probably hindered and it was of interest to distinguish between the two possible rotamers of fujenal (**195** and **196**). The investigation by Hanson and White[97] gave an evidence for the prevalence of the rotamer **195** in the ground state of fujenal. The transformation of steviol (**197**) into *ent*-6β, 7α, 13-trihydroxykaur-16-en-19, 6β-olide (**198**) by *Gibberella fujikuroi* was reported by the same authors.[98] Doubly-labelled 4R-[4^{3}H and 2-^{14}C]-mevalonic acid lactone was fed to *Gibberella fujikuroi*. 7, 18-Dihydroxy-kaurenolide and gibberellic acid were isolated. Whereas the kaurenolide retained all the tritium of the parent mevalonate, the gibberellic acid had lost one tritium atom. From this result and degradation experiment the following conclusions could be drawn. i) The C-9-hydrogen atom of the tetracyclic diterpenes remains throughout the cyclization stages including the formation of ring D, and a $\Delta^{8(9)}$-pimaradiene is excluded at this stage. ii) During the elimination of a C-20 substituent and the formation of the lactone ring of the gibberellins a $\Delta^{10(9)}$ or $\Delta^{10(5)}$ olefin is precluded, because both the 9 and 5-tritiums are retained. iii) Cyclization of a geranylgeranylpyrophosphate derived from 4R-[4^{3}H]-mevalonic acid lactone would be expected to produce an axial tritium atom at position 3 in a kauranoid precursor. Since this atom is retained in gibberellic acid, inversion must have taken place at this center on hydroxylation.[99]

The total synthesis of *rac*-kaur-16-en-19-oic acid (as **199**), *rac*-monogynol (as **200**) and some oxygenated kauranes, chemically and biologically interesting tetracyclic diterpenes, was accomplished by Mori and Matsui[100] as shown in Chart 3. Preparation of some lactones of podocarpane and kaurane series from tricyclic or tetracyclic resin and analogs was described by the same authors.[101] A tetrahydrofurano-hydrophenanthrene derivative was synthesized in the synthetic studies on cafestol.[102] *ent*-19-Nor-16β-kaurane (**201**) and *ent*-19-nor-kaurane (**202**)

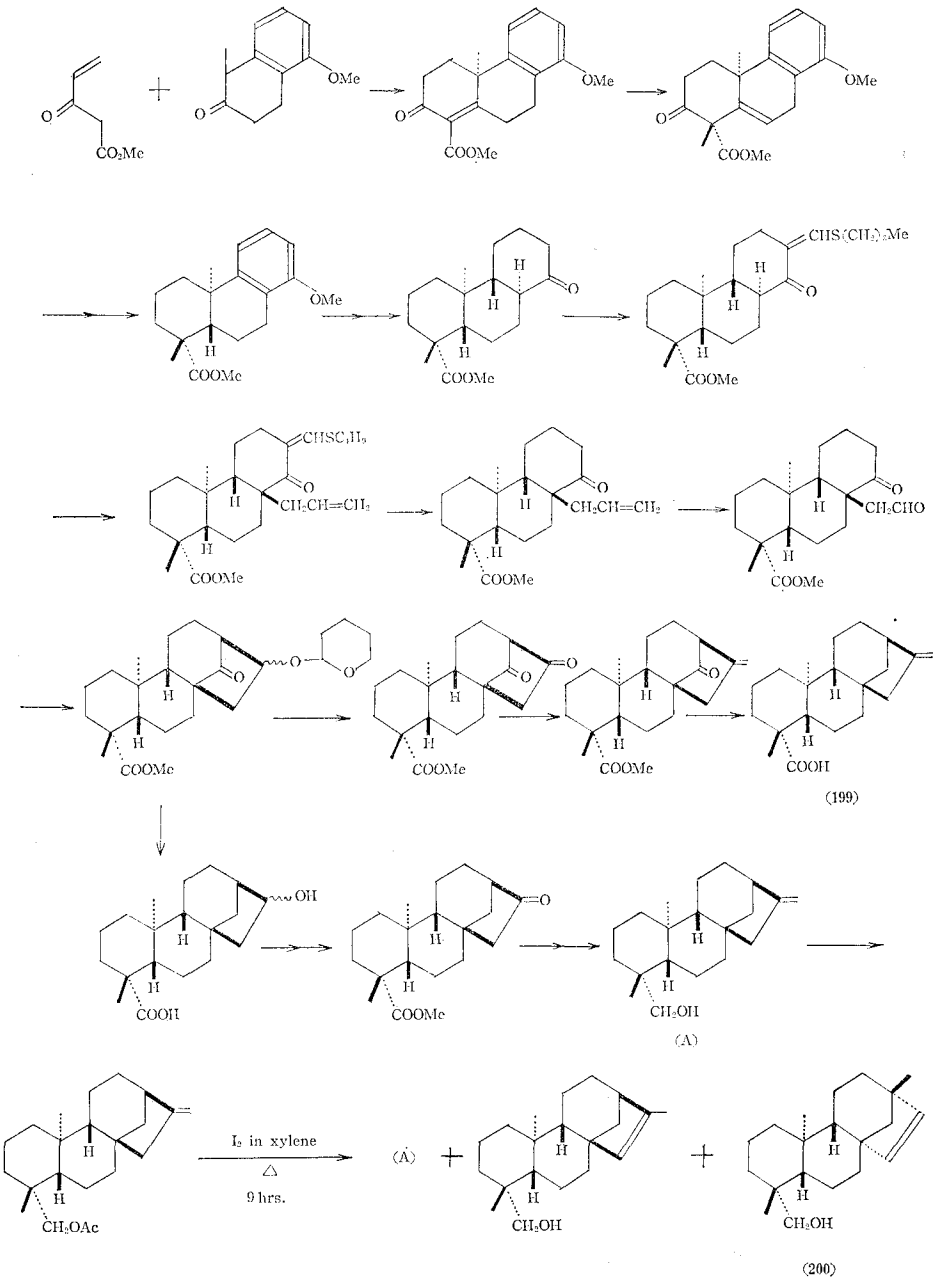
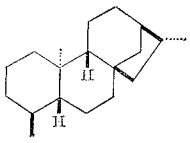
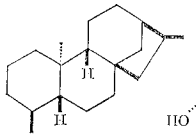


Chart 3

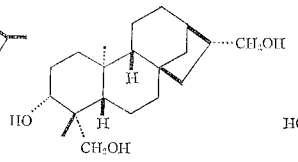
were prepared from *ent*-16β-kaurane-3β, 17, 19-triol (**203**) and *ent*-16-kaurene-3β, 19-diol (**204**) through unambiguous route, and the products were proved to be identical with the samples derived from atractyligenin (**205**).[103] The stereochemistry, especially that of C-9, of atractylanic acid (**206**),[104] which was derived from atractyligenin, was confirmed by a partial synthesis from 7, 18-dihydroxykaurenolide (**207**).[104] A full paper on the synthesis of (−)-6-methyl-7-oxo-bicyclo [3, 2,



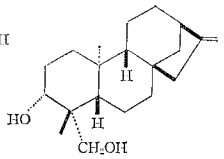
(201)



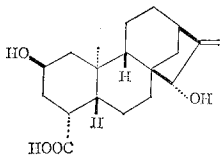
(202)



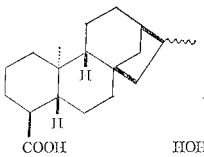
(203)



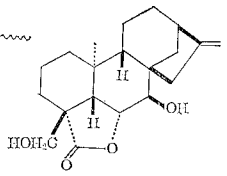
(204)



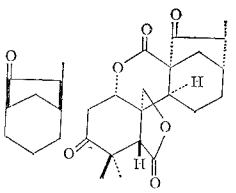
(205)



(206)

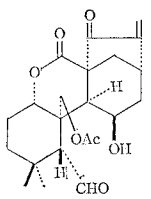


(207)

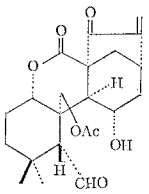


(208) (209)

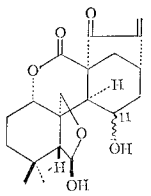
1] octane (**208**), the antipodal substance of a pyrolysis product of bisdehydrodihydroenmein (**209**), was published by Uyeo *et al.*[105] On the basis of spectral data and biogenetic considerations the structure **210** had been deduced by Fujita *et al.*[106] for trichodonin isolated from *Isodon trichocarpus*. Kubota and Kubo[107] isolated the same compound from *I. japonicus* and confirmed unambiguously this



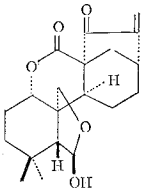
(210)



(211)

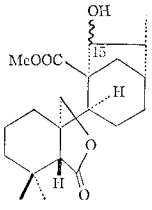


(212) : 11α-OH
(213) : 11β-OH

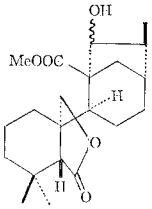


(214)

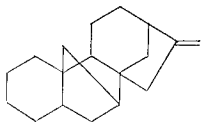
structural assignment by correlating trichodonin with isodonal (**211**) which is also present in *I. japonicus*. They also isolated a new diterpenoid epinodosin (**212**), which is the C-11 epimer of the known nodosin. The full papers which deal with the structure and absolute configuration of nodosin (**213**)[108] and isodocarpin (**214**)[109] were published by Fujita *et al.* Four possible epimeric alcohols **215**~**218**



(215) : 15α-OH
(216) : 15β-OH

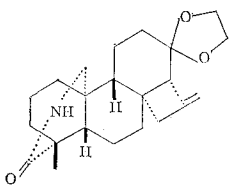


(217) : 15β-OH
(218) : 15α-OH

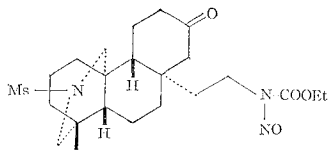


(219)

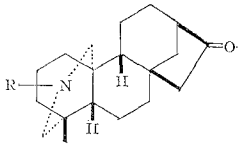
were partially synthesized, and the interesting epimerizations of **215** to **216** and of **217** to **218** were discussed.[110] A review on the diterpenoids of "Enmeiso" was published in Japanese.[111] Another review about the chemistry on diterpenoids of *Isodon* species was published in English by Fujita.[112] The carbon skeleton **219** was deduced for vakognavine, an alkaloid of *Aconitum palmatum*.[113] A new simple synthesis of veatchine from **220** was reported by Wiesner *et al.*[114] The



(220)

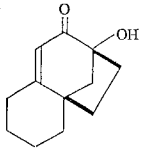


(221)

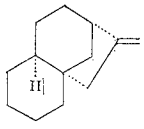


(222) : R=Ms
(223) : R=Ac

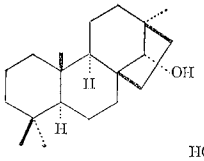
compound **220** was converted into **221**, which was treated with sodium ethoxide in refluxing ethanol to give **222**. The latter was transformed through a series of reactions into **223**, which had been converted into veatchine. A conjugated ketone **224** was synthesized, then the compound was transformed into **225**.[115]



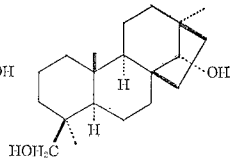
(224)



(225)

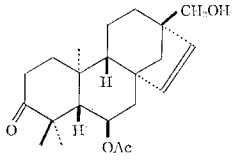


(226)

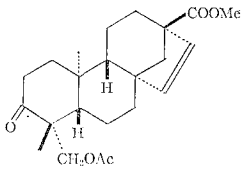


(227)

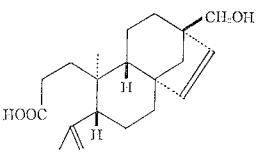
Manool and agathadiol cyclize in formic acid to 14α-hydroxybeyerane derivatives **226** and **227** besides pimarane derivatives.[39,55]* Three new diterpenes, which were correlated with beyerol and were shown to be modified *ent*-beyer-15-enes **228**, **229**, and **230**, were yielded from a variety of *Beyeria leschenaultii*.[116] The



(228)



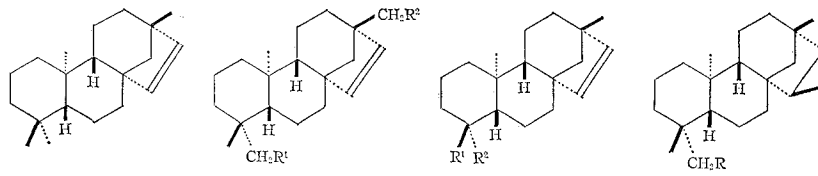
(229)



(230)

structure and stereochemistry of *ent*-hibaene (**231**), erythroxylol A (**232**), erythroxylol B (**233**), and erythroxydiol A (**234**) were assigned on the basis of spectroscopic properties and chemical reactions.[117] Erythroxydiol A (**234**) was

* See also section III.



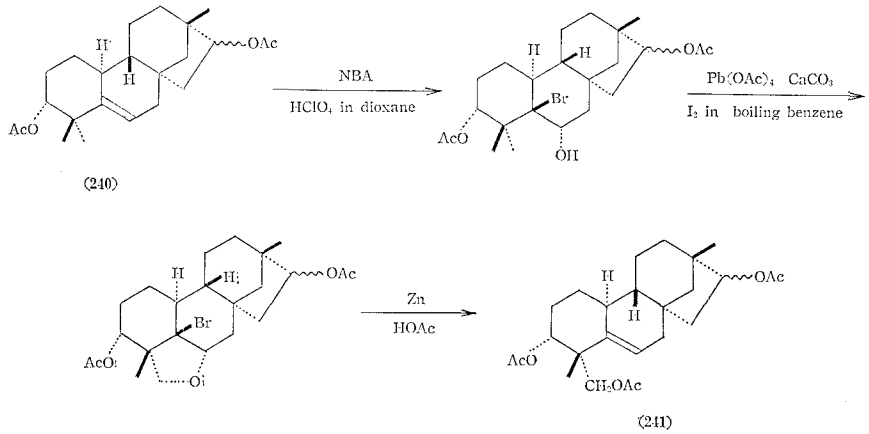
(231)

(232) : R^1=OH, R^2=H
(233) : R^1=H, R^2=OH
(234) : R^1=R^2=OH

(235) : R^1=OH, R^2=Me
(236) : R^1=Me, R^2=OH

(237) : R=H
(238) : R=OH
(239) : R=OAc

converted into erythroxylol A (232), and erythroxylol A (monogynol) (232) and B (233) were converted into *ent*-hibaene (231). Two norditerpenoid tertiary alcohols, 235 and 236, and three diterpenoid epoxides, 237, 238, and 239, were isolated from *Erythroxylon monogynum*.[118] Compound 241, a potential intermediate for synthesis of gibberellins, was derived from 240 through a route shown in Chart 4 by Mori, Matsui *et al.*[119] The biogenetic-like rearrangements of isosteviol de-

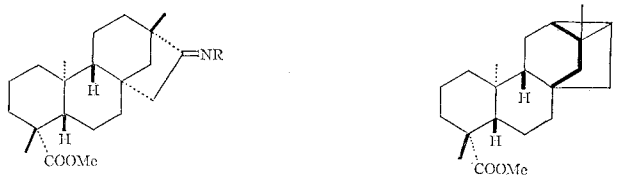


(240)

(241)

Chart 4

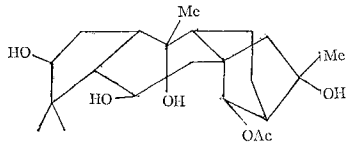
rivatives 242 and 243 were carried out to give several products, among which methyl trachyloban-19-oate (244) was found from the reaction of 242 (as its sodium salt) in 10 % ethylene glycol diethylcarbitol at 180~190°.[120] Stereochem-



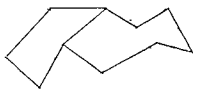
(242) : R=NHTs
(243) : R=OH

(244)

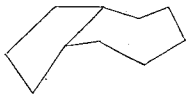
istry of grayanotoxin I was investigated more in detail and the stereochemical structure 245 with the 246 (not 247) type hydroazulene was presented.[121]



(245)



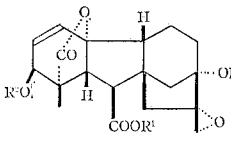
(246)



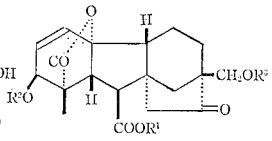
(247)

IX. GIBBERELLANE DERIVATIVES

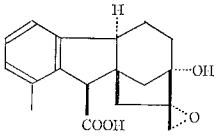
Gibberellic acid 16 S, 17-epoxide (**248**) and its acetate (**249**) were converted by Wagner-Meerwein's rearrangement into hydroxymethyl derivatives **250** and **251**, respectively. *Allo*-gibberic acid 16 S, 17-epoxide (**252**) was rearranged to **253**.[122] Gibberellin A_{16}, a new metabolite of *Gibberella fujikuroi*, was isolated as



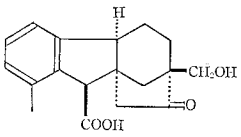
(248) : R^1=R^2=H
(249) : R^1=H, R^2=Ac



(250) : R^1=R^2=R^3=H
(251) : R^1=R^3=H, R^2=Ac

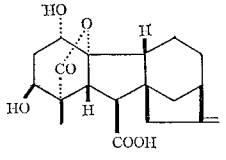


(252)

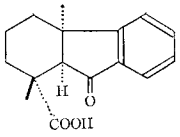


(253)

the methyl ester, and the structure (**254**) was elucidated.[123] An intermediate (as **255**) for synthesis of gibberellins was synthesized as racemic compound.[124] Fragmentation patterns of gibberellin A_4 methyl ester (**256**) and its 3-keto-1-13-



(254)



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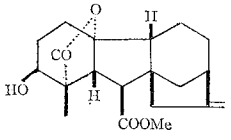
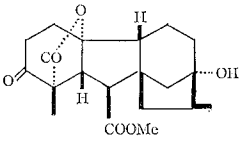
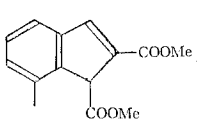


(256)

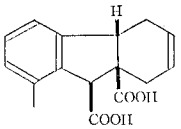


(257)

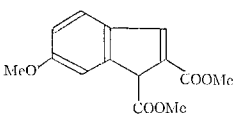
hydroxy-16, 17-dihydro analog (**257**) as well as mass spectra of some Δ^1- and $\Delta^{1(10)}$-unsaturated compounds of gibberellin series were investigated. Gibberellin derivatives unsaturated in the ring A gave different mass spectra, depending on the position of the double bond. This is useful for the determination of the position of double bond.[125] 1, 2-Dicarbomethoxy-7-methylindene (**258**) was synthesized. Its Diels-Alder reaction with butadiene yielded tetrahydrofluorene derivative **259**.[126] The double bond isomers of 1, 2-dicarbomethoxy-6-methoxyindene, **260** and **261**,



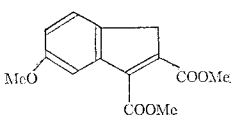
(258)



(259)

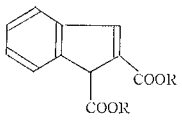


(260)

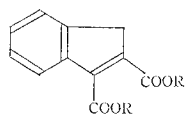


(261)

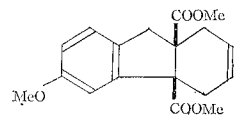
and another pair of 1, 2-dicarbomethoxyindene, **262** and **263**, were synthesized. In each case, the less highly substituted double bond isomer **260** or **262** is the more stable. However, derivatives of each of these indenes reacted with 1, 3-butadiene to give the Diels-Alder adduct (**264** and **265**) derived from the more



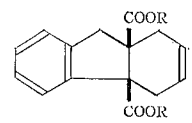
(262) a: R=Et
b: R=Me



(263) a: R=Et
b: R=Me



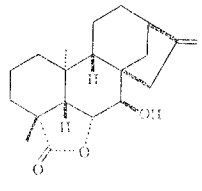
(261)



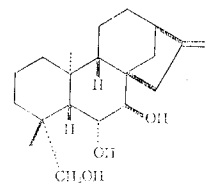
(265)

highly substituted double-bond isomer.[127]

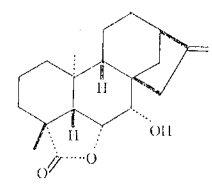
None of 7-hydroxykaurenolide (**266**), its related triol (**267**) and 7α-hydroxykaurenolide (**268**) was incorporated into gibberellic acid by *Gibberella fujikuroi*, but 7-hydroxykaurenolide (**266**) was converted into 7, 18-dihydroxykaurenolide (**269**) in high yield. Incorporation of alcohol **270** into gibberellic acid was much higher than that of diene **271**.[128] Seven ^{14}C-labelled compounds, including gibberel-



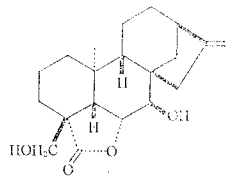
(266)



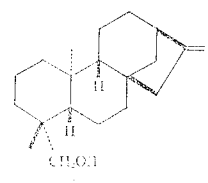
(267)



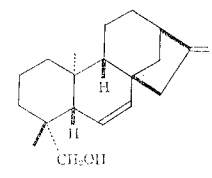
(268)



(269)



(270)



(271)

lins A_{12}, A_{13} and A_{14}, were prepared and tested as precursors in the biosynthesis of gibberellic acid by *Gibberella fujikuroi*. It was suggested by Cross *et al.*[124] that gibberellic acid is biosynthesized from *ent*-kaurene ((−)-kaurene) through **272** and gibberellin A_{14} (**274**) or the corresponding 7-aldehyde **273**. Gibberellin A_{13} (**275**) was not thought to be a precursor of gibberellic acid. The biosynthetic pathway suggested by them is shown in Chart 5. Although several kaurene derivatives, **276**, **277** and **278** having the 16-methylene group, undergo ring contraction to gibberellanes, *e. g.* **279**, with base, those having a 16-keto-group, **280** and **281** do not. The fact was considered to be due to a long-range effect associated with the 16-keto-group.[129] Methyl 3-dehydrogibberellate (**282**) was treated with zinc in acetic acid and then with aqueous sodium bicarbonate to give a reductive delactonized product **283**.[130] The presence of three water-soluble

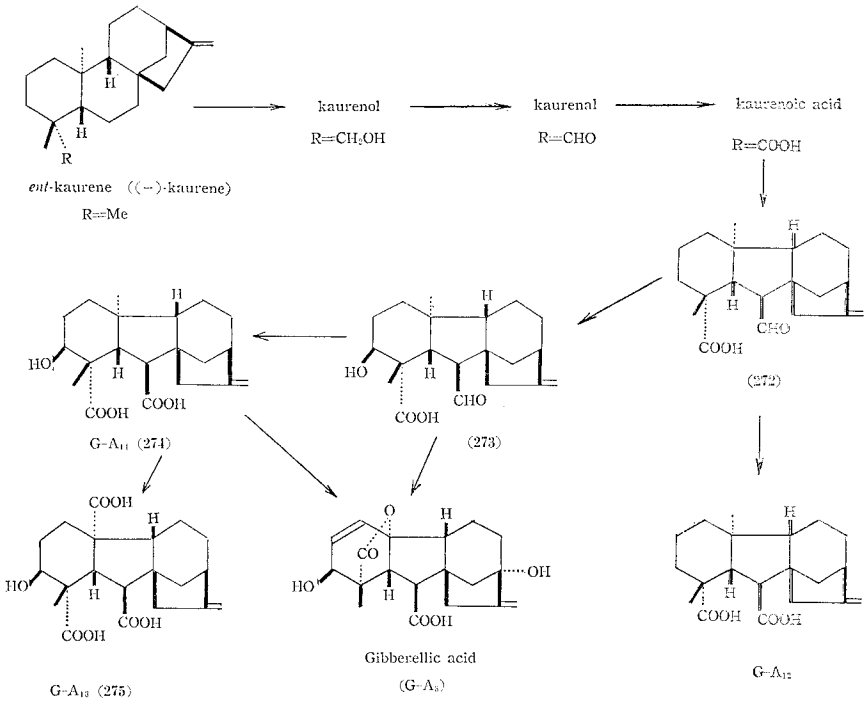
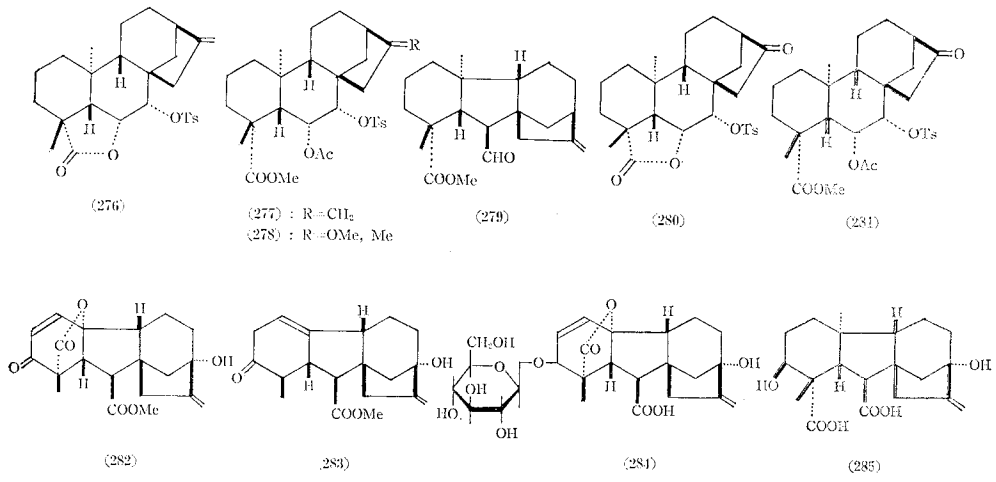


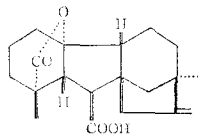
Chart 5



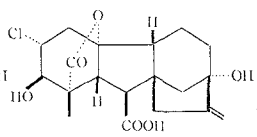
gibberellins was confirmed in immature seeds of morning glory (*Pharbitis nil*). The structure of the main component was elucidated as 3-*O*-β-glucosyl-gibberellin A_3 (**284**).[131] A short review about isolation of new gibberellins from higher plants and their biological activity was published. It is concerned with Bamboo gibberellin, *Pharbitis* gibberellin, gibberellin A_3 glucoside (**284**), and *Canavalia* gibberellins I and II.[132] A new gibberellin, tentatively called *Lupinus* gibberellin I, was isolated from young yellow lupin seeds (*Lupinus luteus*). It was shown

to have structure (285).[133]

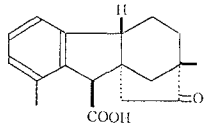
A new nomenclature of gibberellins was proposed.[134] According to this, *Lupinus* gibberellin-I, Bamboo gibberellin, *Pharbitis* gibberellin, *Canavalia* gibberellin-I and -II were named gibberellins A_{18}, A_{19}, A_{20}, A_{21} and A_{22}, respectively. A review on the isolation techniques of plant growth substances was published, in which purification of bamboo gibberellin by counter-current distribution and isolation of gibberellins A_1 and A_3 by partition chromatography were described.[135] Gibberellin A_{23}, that is, gibberellin A_3 glucoside (284) was isolated from immature seeds of *Lupinus luteus*.[136] Investigations of gibberellins in *Phaseolus multiflorus* by combined gas chromatography-mass spectrometry have been carried out by MacMillan *et al.* They[137] reported the detection of gibberellin A_{20} (*Pharbitis* gibberellin) (286) in extracts of young seed of the plant and some observations on the structures of compounds *a* and *b*, previously isolated from seeds of *P.*



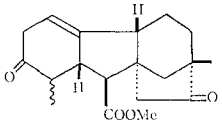
(286)



(287)



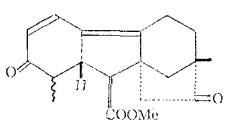
(288)



(289)

multiflorus by Jones.[138] The investigation provided strong support for the structure 287, originally suggested for compound *b* by Jones.

Mori, Matsui, Sumiki, *et al.*[139,140] converted *rac*-epigibberic acid (as 288), which had been synthesized by themselves, into 290 *via* an important intermediate 289. Since the ketone 290 had been converted into gibberellin C (291) by



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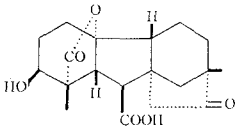

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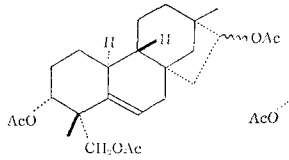

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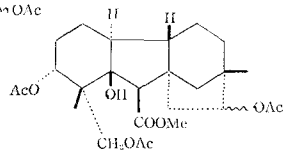
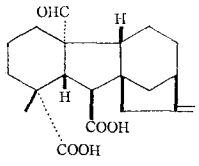


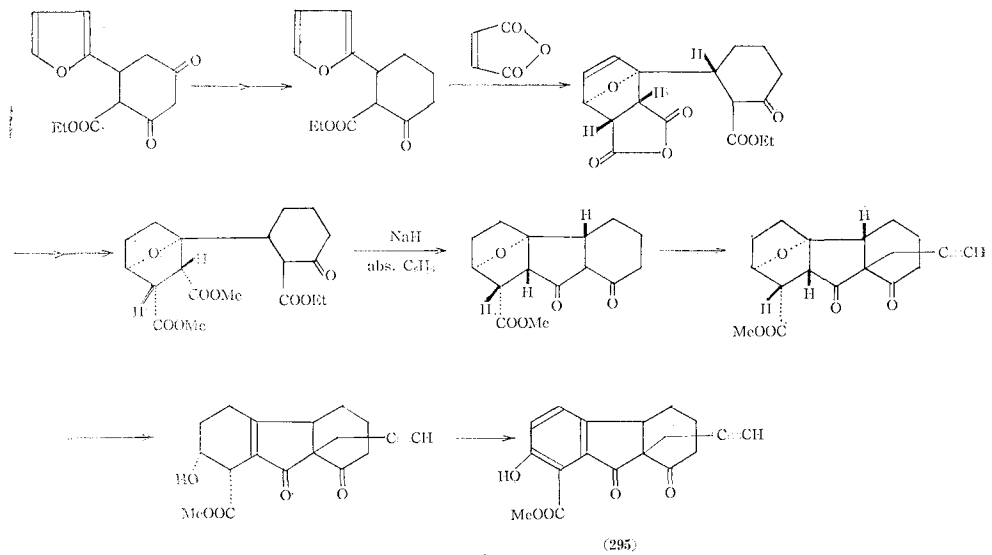
(293)

them,[141] this completed total synthesis of *rac*-gibberellin C. Gibberellin C had been transformed into gibberellin A_4,[142] which had been converted into gibberellins A_2[143] and A_9.[144] Conversion of gibberellin A_9 into A_{10} had also been reported.[145] Thus, the foregoing work constituted the formal total synthesis of *rac*-gibberellins A_2, A_4, A_9 and A_{10}. The same group[146] reported the synthetic sequence for the conversion of compound 292 into 293. Gibberellin A_{24} (294), a new aldehydic



(294)

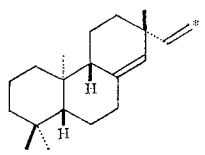
gibberellin was isolated from *Gibberella fujikuroi*.[147] Circular dichroism of some C_{19} gibberellins and their methyl esters, and some other related compounds at wave length of 200~300 mμ was investigated and the application of the lactone chromophore to their structural and stereochemical elucidation was described.[148] The synthesis of perhydrofluorenone derivative **295** was reported by Kitahara *et al.*[149] The outline of the route is shown in Chart 6.



(295)

Chart 6

Cross and Stewart[150] reported that addition of the labelled *ent*-pimara-8(14), 15-diene (**296**) to a fermentation of *Gibberella fujikuroi*, and isolation of the metabolites produced, gave labelled methyl gibberellate (incorporation 0.05 %) and labelled 7-hydroxykaurenolide. Hanson and White[151] proved by feeding [2-$^3H_2$, 2-^{14}C] mevalonic acid lactone to *Gibberella fujikuroi* that *ent*-pimara-8(14), 15-diene (**296**) is a precursor for *ent*-kaurene, 7-hydroxykaurenolide, and 7, 18-

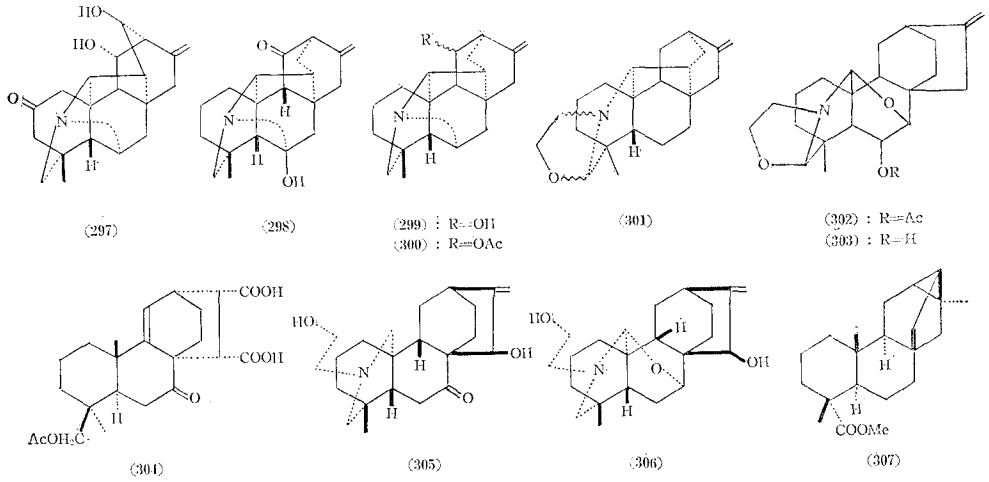


(296)

dihydroxykaurenolide. They also prepared labelled *ent*-pimara-8(14), 15-diene (**296**) (^{14}C and ^3H), and carried out feeding experiments to *Gibberella fujikuroi*. Its very low incorporation (0.02 %) to gibberellic acid was observed. Decarboxylation of C_{20} gibberellin to C_{19} gibberellin was discussed on the basis of multiple labelled mevalonate experimental results. Subsequently, Cross and Stewart[152] revised their foregoing report. They described that pimaradiene and pimaradienol are not incorporated into gibberellic acid, on the basis of the degradation experiments.

X. ATISANE DERIVATIVES

The tentative structure **297** previously proposed for an alkaloid isolated from *Delphinium cardinale* was confirmed.[153] The alkaloid is identical with hetisinone, which was first obtained as the transformation product of hetisine and later isolated from *D. denudatum*. Ten alkaloids were isolated from *Spiraea japonica* and the structure **298** of spiradine A was elucidated by X-ray analysis. The structures **299** and **300**, were assigned to spiradine B and C, respectively, based on the chemical correlation with A.[154] Subsequently, spiradine D isolated from the same plant source proved to be represented as **301**.[155] The plane structures, **302** and **303**, were proposed for spiradines F and G, respectively.[156] A key intermediate **304** in the synthesis of atidine (**305**) and ajaconine (**306**) was prepared.[157]



The synthesis of methyl 13, 16-cycloatisan-18-oate (methyl *anti*-trachylobanate) (**307**) from methyl levopimarate was reported by Herz *et al.*[158,159] The compound **308** which was derived from the starting material *via* Diels-Alder reaction was converted into **309** by the mesylation, and the latter was transformed into the final product as shown in the Chart 7.

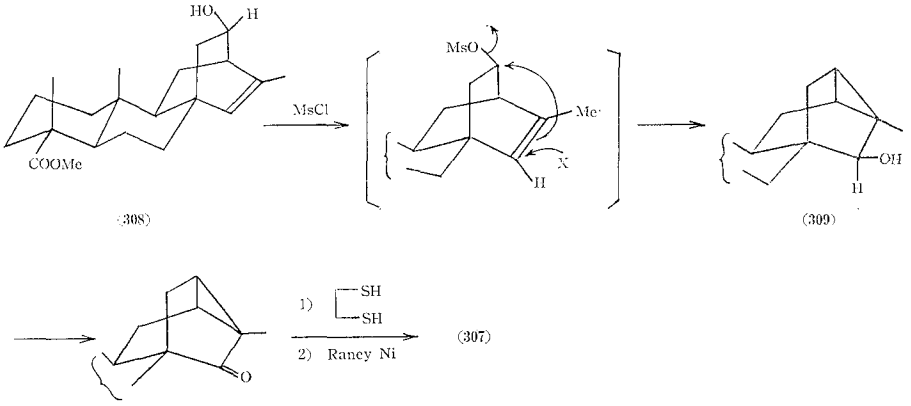
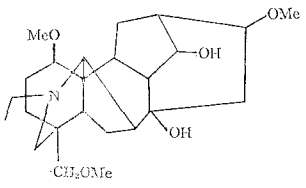


Chart 7

XI. ACONANE DERIVATIVES

On the basis of mass spectrometry, the NMR data of acetylbenzoyl derivative, and the NMR data of the product prepared from pyrolysis of diacetyl derivative, the formula **310** was proposed for talatizamine.[160] The structure of jesaconitine



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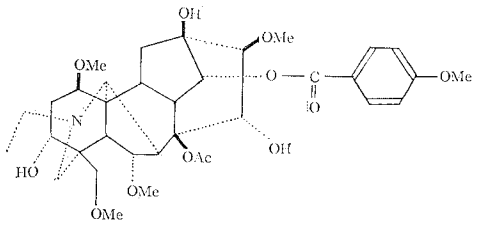
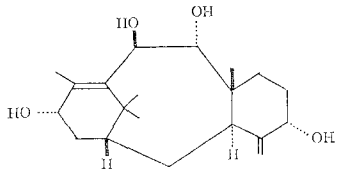


(311)

isolated from *Aconitum* species was elucidated as **311**, on the basis of the NMR data of the alkaloid and its pyrolysis products. The pyrolysis was carried out in an NMR tube, and continuously monitored by NMR spectroscopy to provide evidence for the elimination product. This method of pyrolysis constituted a rapid and convenient way of establishing the presence of certain C-8 ester groups in these diterpene alkaloids using small amounts of material.[161]

XII. TAXANE DERIVATIVES

A constituent of the heartwood of *Taxus cuspidata* was isolated and named taxusin.[162] Hydrolysis of taxusin gave tetraol **312**, which had been isolated from *T. baccata* by English workers.[163] The application of Mills' rule gave same conclusion on the absolute configuration of C-13 hydroxy group. Taxusin corresponds to tetraacetate of **312**.[162]

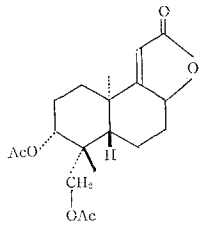


(312)

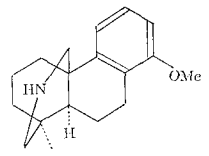
XIII. THE OTHERS

Johnson[164] published a review on nonenzymic biogenetic-like olefinic cyclizations. The ORD curves of many diterpenecarboxylic acids and related compounds were taken and examined by English workers.[165] Discussions on preferred conformations of carboxylic acids and carboxyl sector rule were described. The NMR investigation on forty four kinds of diterpene alkaloids and related compounds was published.[166] On the basis of the NMR data of C-4 methyl group in a series of atisine and veatchine, the conformation of ring E was discussed. The relationship between the chemical shift of C-4 methyl protons and nitrogen

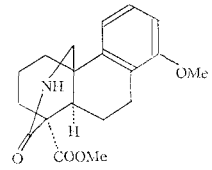
atom was also discussed. The conformation of the primary hydroxy group at C-18 or C-19 in many diterpenoids was discussed on the basis of the chemical shift of C-4 methyl protons' signal in the NMR spectra.[167] Similarly, the conformation of C-4 axial and equatorial carboxylic acids, esters, and aldehydes in diterpenoids was discussed on the basis of NMR data of C-10 methyl group.[168] The NMR spectra and conformations of some lactones of octa- and decahydro-8-hydroxy-naphthoic acids were discussed,[169] on relation to synthesis of diterpenoid acids. A ten-step stereoselective synthesis of racemic andrographolide lactone (as **313**), which had been obtained previously in optically active form by degradation of triacetylandrographolide, was published.[170]



(313)



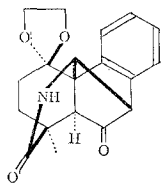
(314)



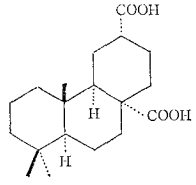
(315)

Turner *et al.*[171] published procedures for the synthesis of tetracyclic intermediates—*e. g.* **314** and **315**—incorporating the bridged nitrogen-containing ring common to many of the diterpene alkaloids.

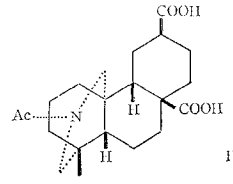
Wiesner *et al.*[172] carried out a stereoselective synthesis of pentacyclic intermediate **316** during the synthesis in the series of diterpene alkaloids. Stereoselective synthesis of racemic tricyclic dicarboxylic acid (as **317**), a synthetic model for the N-acetyl-dicarboxylic acid **318**, was reported by Pelletier *et al.*[173] Stereoselective synthesis of racemic perhydrophenanthrene derivative (as **319**) was



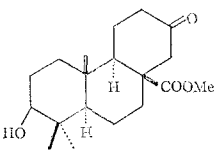
(316)



(317)

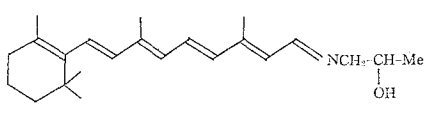


(318)



(319)

reported by Dutta *et al.*[174] Spectral properties of Schiff bases of retinal were investigated. 1-(Retinylideneamino)-2-propanol (**320**) and its 11-*cis* isomer were prepared by condensing retinal with 1-amino-2-propanol in dry acetonitrile, and



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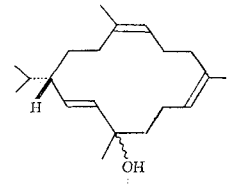
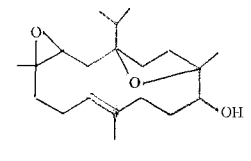
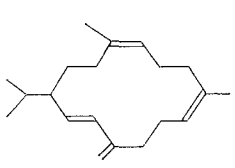


(321)

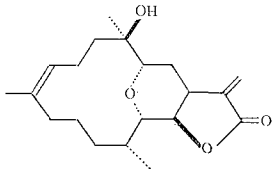


(322)

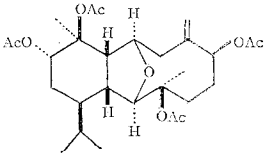
λ_{max} in non polar solvent was discussed.[175] Thunbergol, a new macrocyclic diterpene alcohol, was isolated from the oleoresin of *Pseudotsuga menziesii*, and structure **321** was assigned to this.[176] A new diterpene, incensole-oxide (**322**), was isolated from the resin produced by *Boswellia carteri*. Chemical and physicochemical data showing the position of the oxirane ring supported the structure.[177] The new diterpenes, isocembrene (**323**) and isocembrol, were isolated from oleo-



(323)

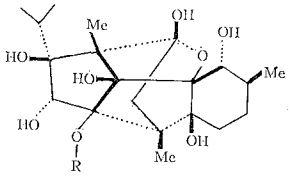


(324)



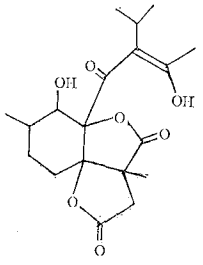
(325)

resin of *Pinus sibirica*.[178] The plane structure of the latter is identical with **321**. The antibacterial marine diterpene eunicin was isolated from *Eunicea mammosa* and characterized,[179] and structure **324** was assigned to it. The assignment was fully substantiated by the X-ray crystallographic study of its iodoacetate.[180] From the petroleum ether extract of dried *Eunicella strica*, a new diterpenoid, eunicellin was isolated. The structure **325** was presented on the basis of chemical evidence and an X-ray analysis of dibromide.[181] The molecular structure of ryanodol *p*-bromo benzyl ether was elucidated as **326** on the basis of X-ray analysis.[182] The structure was identical with that proposed by Wiesner *et al.*[183] except that the configuration of the carbon atom carrying the isopropyl group in the five-membered ring is reversed. An article, which represents the English version of the second

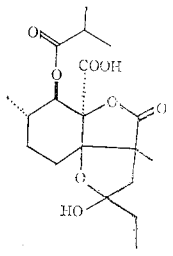


(326) : R=$-CH_2-C_6H_4-Br$

(327) : R=$-C(=O)-C_4H_3NH$



(328)

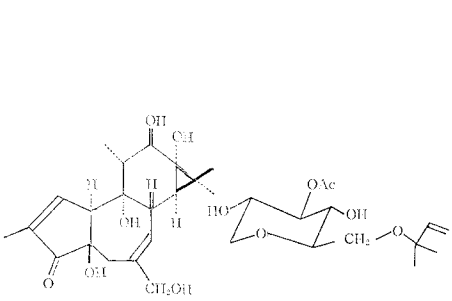


(329)

part of a lecture on the structure of ryanodine (**327**) delivered by Wiesner[184] in 1967, in the auditorium of the Institute for Org. Chem. and Biochemistry, Czechoslovak Academy of Sciences, was published. Ryanodol was treated with excess periodate and then alkali to give a C_{19} compound, whose structure **328** was proposed on the basis of the several reactions.[185] The structure **329** was proposed for a C_{19} acid obtained together with the foregoing ketone in the periodate oxidation of ryanodol.[186]

Hecker *et al.* published a series of the reports on the chemistry of phorbol. They were concerned with polybenzoate and polyacetate of phorbol and phorbol-3-ol, functional derivatives of allyl-group of phorbol,[187] ether derivatives of

phorbol,[188] derivatives of phorbol-12-one and their circular dichroism,[189] the α, β-unsaturated tertiary 1, 2-ketogroup in phorbol,[190] and the oxidation of phorbol with leadtetraacetate.[191] Another report on the chemistry and structure of phorbol was published by Crombie *et al.*[192] The structure and absolute configuration **330** have been established by the X-ray analysis of its bromine-containing derivative.[193]



(330)

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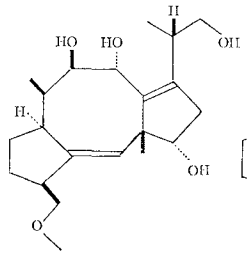

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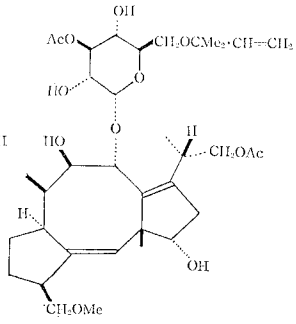
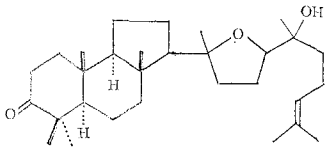


(333)

Characterization of the oxygen substituents of fusicoccin (fusicoccin A), $C_{38}H_{58}O_{13}$, a highly phytotoxic metabolite of *Fusicoccum amygdali*, led to a partial structure **331**.[194] Crystallographic studies of two mercuribromide derivatives prepared from fusicoccin and its deacetylaglycone resulted in the presentation of the structure and relative stereochemistry **332** for deacetyl aglycone.[195] On the basis of chemical works and X-ray data, Barton *et al.*[196] presented the complete structure **333** including absolute configuration. These results were completely identical with those of the independent work on fusicoccin A by Ballio and his colleagues.[197] They carried out an X-ray determination of the structure of the iodobenzenesulfonate of fusicoccin with supporting chemistry.

d-Malabaricol (**334**) was converted into *d*-ambreinolide (**335**).[198] A biosynthetic study with viridin (**336**), an active antifungal metabolic product of *Gliocladium*



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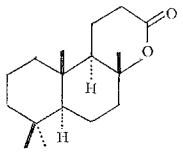

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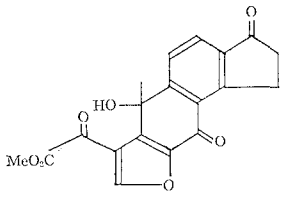

(336)

virens, led to a conclusion that the metabolite is biosynthesized from mevalonic acid lactone by way of farnesyl pyrophosphate, squalene epoxide, and lanosterol, and excluded the possibility that the compound might be derived from mevalonic acid *via* geranylgeranyl pyrophosphate and a tricyclic diterpenoid (cassane type skeleton).[199] The biosynthesis of pleuromutilin, a metabolite from *Pleurotus mutilus*, was described by Arigoni.[200]

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