

Review

The Chemistry on Diterpenoids in 1976

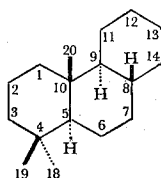
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Manabu NODE, and Masahito OCHIAI

Received November 2, 1977

I. INTRODUCTION

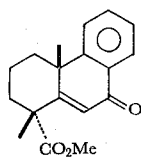
This is one of a series of our annual reviews¹⁾ on diterpenoids chemistry. The classification of the compounds is the same as that which has been used in our reviews since 1969.

II. PODOCARPANE DERIVATIVES

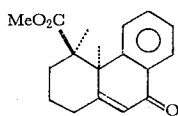


Podocarpane

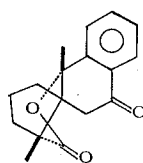
Rearrangement of deisopropyl phenacylidene type diterpene by means of aluminum chloride was investigated. Thus, the reaction of **1** with aluminum chloride in anhydrous benzene gave the rearranged ester **2**, as a major product, in company



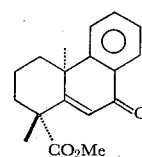
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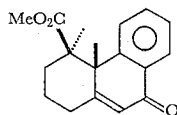
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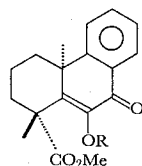
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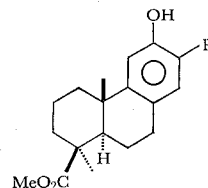
(4)



(5)



(6) R=Ac
(7) R=H

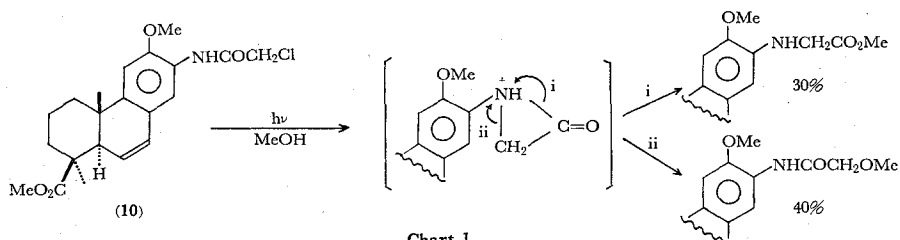


(8) R=H
(9) R=I

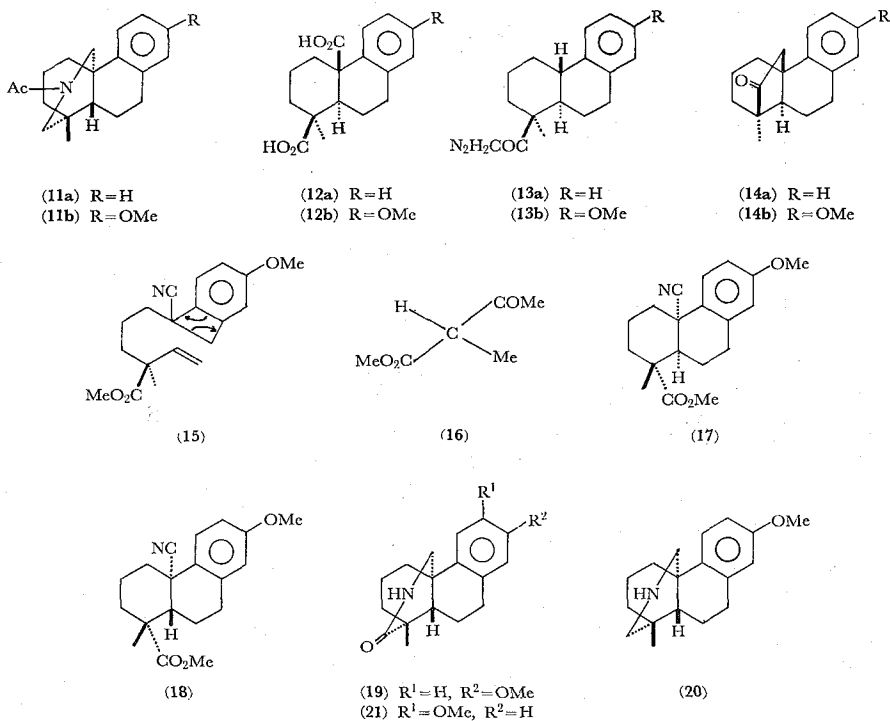
* 藤田栄一, 富士 薫, 長尾善光, 野出 学, 落合正仁: Laboratory of Physiological Activity, Institute for Chemical Research, Kyoto University, Uji, Kyoto-Fu 611, Japan.

with the γ -lactone **3**. On the other hand, the reaction of **4** afforded a large portion of the starting material in company with a small amount of the rearranged ester **5**. Next, the reaction of the enol acetate **6** gave only the enol **7** in the accompany of deacetylation²⁾. Treatment of a phenol **8** with thallium (I) acetate and iodine gave a selective *ortho*-iodinated product **9**.³⁾

N-Chloroacetylamine **10** on photolysis in methanol afforded the rearranged N-substituted glycine ester along with the unrearranged methyl ether.⁴⁾ (Chart 1)



A new stereocontrolled synthetic route to some intermediates (**11a, b** and **12a, b**) for diterpenoid alkaloids and C₂₀ gibberellins was published. The synthetic approach contains a novel method of angular alkylation based upon a regioselective intramolecular α -oxocarbenoid insertion across the benzylic C-H (at C-10) bond in the copper-catalyzed carbenoid decomposition of the easily accessible α -diazomethyl ketone **13a** and **13b** to the corresponding bridged tetracyclic ketones **14a** and **14b**.⁵⁾



A facile regiospecific and stereocontrolled synthesis of a diterpene alkaloid intermediate from benzocyclobutenes was reported. Namely, thermolysis of **15** derived from methyl methacetoacetate **16** in five steps gave phenanthrene derivative **17**, which was converted into the epimer **18** by oxidation, bromination, dehydrobromination, and hydrogenation. Catalytic reduction of **18** gave the lactam **19**, whose reduction with LiAlH_4 afforded imine **20**.⁶⁾ Similarly, compound **21** was synthesized.⁷⁾

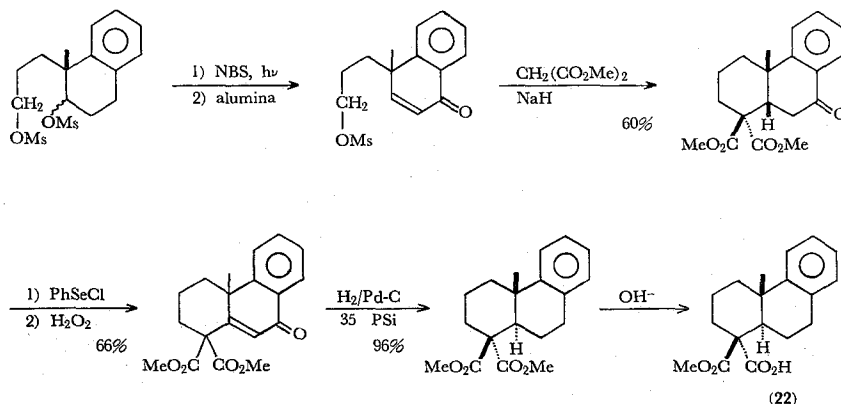
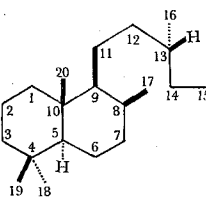


Chart 2

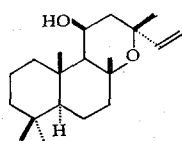
An efficient stereoselective synthesis of a tricyclic intermediate **22** for the synthesis of derivatives of abietic and podocarpic acid was reported.⁸⁾ (Chart 2)

III. LABDANE DERIVATIVES

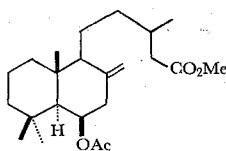


Labdane

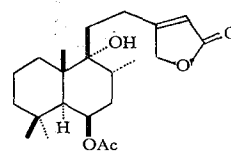
11 β -Hydroxymanoyl oxide (**23**) was isolated from *Juniperus oxycedrus* together with other diterpenes.⁹⁾ From *Cistus hirsutus*, methyl ester **24** of 6 β -acetoxyadenic acid was isolated.¹⁰⁾ Labd-8(20),13-dien-15-ol, (+)-manoyl oxide, epimanoyl oxide, *cis*-abienol, and 7 α -hydroxydehydroabienol were isolated from the resin of



(23)



(24)

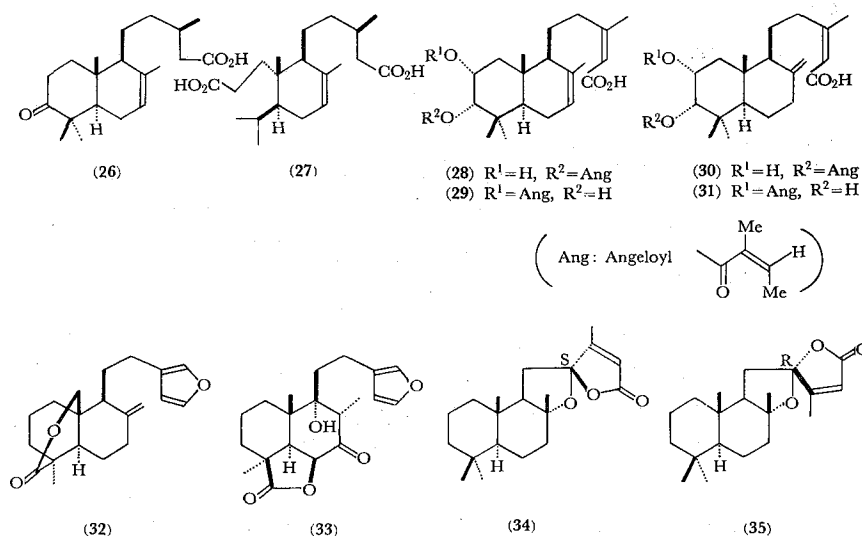


(25)

Pinus koraiensis and their identities confirmed by chemical and spectral methods.¹¹⁾ A new diterpenoid, named vitexilactone, was isolated from the leaves of *Vitex cannabifolia* and its structure was established as 25 by the chemical and spectral examination.¹²⁾

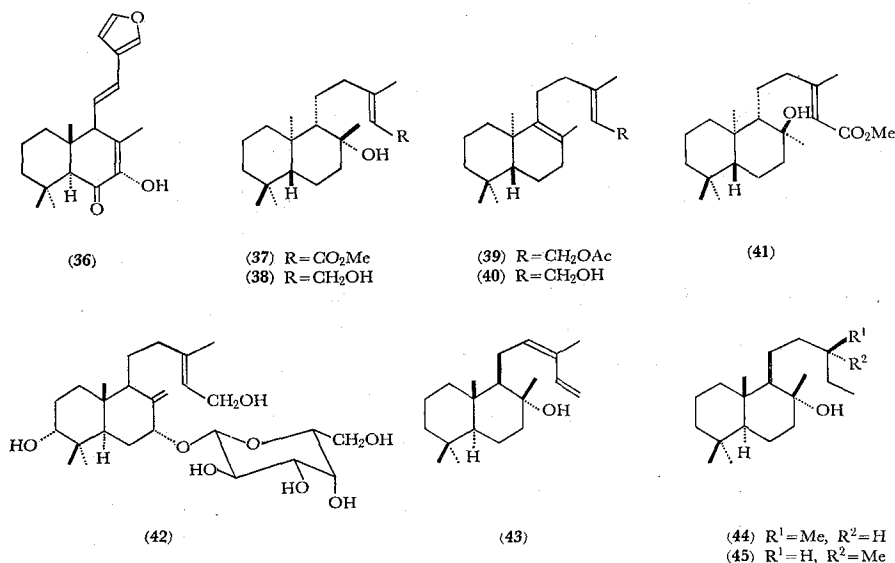
Several new diterpenes, 26, 27, 28, 29, 30, and 31, were isolated from the plants of the genus *Brickellia*. Compound 27 is a new type of degraded diterpene which, however, is closely related to 26.¹³⁾

A new furanoid diterpene, potamogetonin (32), was isolated from seeds of *Potamogeton ferrugineus*. The structure was assigned on the basis of its spectral characteristics, particularly by NMR.¹⁴⁾ Structure of ballotinone, a diterpenoid from *Ballota nigra*, was established on the basis of its ¹³C NMR spectrum to be 7-oxomarrubiin (33) [15, 16-epoxy-9-hydroxy-7-oxo-8 β H-labda-13(16), 14-dien-19, 6 β -olactone].¹⁵⁾ Giles and Schumacher¹⁶⁾ had proposed structures 34 and 35 for β - and α -levantenolide, respectively. However, it was reported that the C-12 stereochemistry of the α -levantenolide, $[\alpha]_D +60.4^\circ$, should be changed to 12 S and that of β -levantenolide, $[\alpha]_D -59.6^\circ$, to 12 R on the basis of their ¹³C FT NMR spectra *etc.*¹⁷⁾

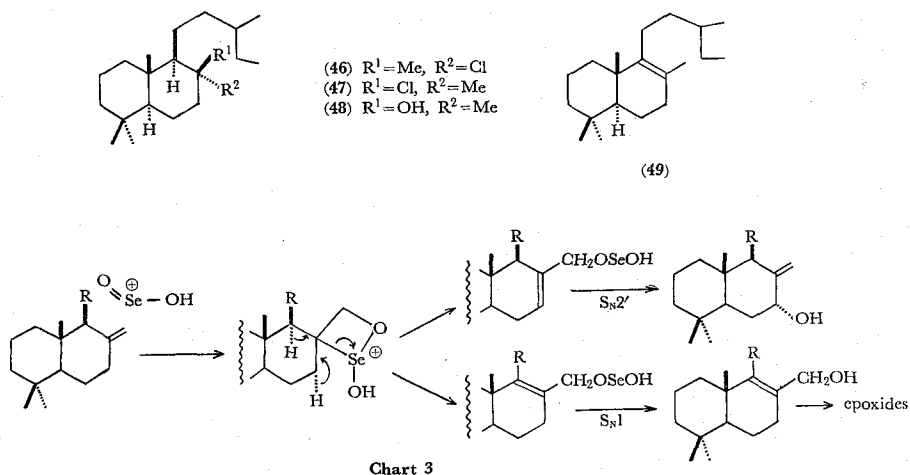


A furanoditerpene was isolated from *Hedychium spicatum*, and it was designated as 7-hydroxyhedychenone (36).¹⁸⁾ Five *ent*-labdane diterpenes were isolated from the neutral fraction of the resin of *Araucaria bidwillii*. Two of the compounds were the already known methyl *ent*-8 β -hydroxy-labd-E-13-en-15-oate (37) and *ent*-8 β , 15-labd-E-13-enediol (38). Three of them, previously unknown, were assigned the structures *ent*-15-acetoxy-labd-8, E-13-diene (39), *ent*-labda-8, E-13-dien-15-ol (40) and methyl *ent*-8 α -hydroxy-labd-E-13-en-15-oate (41).¹⁹⁾

A new diterpene galactoside, named acanthospermol- β -galactosidopyranoside, was isolated from *Acanthospermum hispidum* and its structure (42) was clarified.²⁰⁾ 13-Epimanool was isolated from *Pinus contorta* bark and *Tsuga heterophylla* wood. Southern pine (*Pinus* spp.) tall oil was found to contain a mixture of manool and 13-epimanool.²¹⁾



It was shown that tetrahydroabienol, which was obtained by hydrogenation of abienol (43), was a quasiracemic compound formed from C-13 epimers. Namely, the compound is a mixture of 44 and 45.²²⁾ The tetrahydroabienol (44 and 45) with phosphorus pentachloride smoothly gave the chloride 46 with less than 5% elimination to olefinic compounds. On the other hand, the C-8 epimeric alcohol 48 with phosphorus pentachloride gave a mixture comprising chloride 47 (40%), chloride 46, and olefin 49.²³⁾

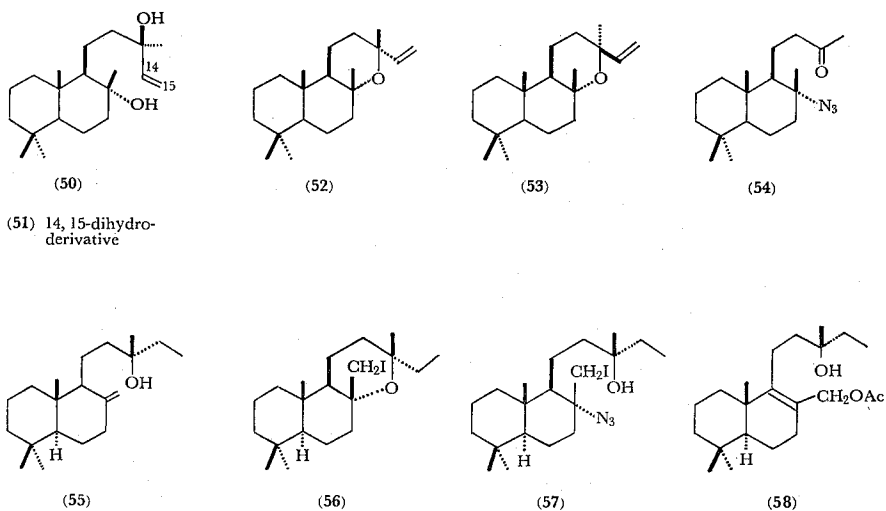


Allylic oxidation of exocyclic olefins with SeO₂/H₂O₂ was investigated and the mechanism was postulated: the reaction would proceed through the intermediacy of an oxaselenocyclobutane to a selenite ester which is solvated by competitive unimolecular (S_N1) and bimolecular (S_N2') processes.²⁴⁾ (Chart 3)[†]

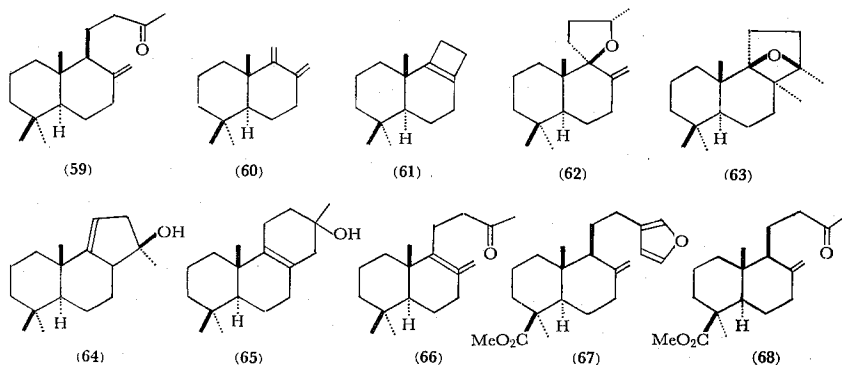
[†] See another mechanism by H. P. Jensen and K. B. Sharpless (*J. Org. Chem.*, **40**, 264 [1975]).

In the synthesis of tertiary azides from sclareol **50** and dihydrosclareol **51**, $\text{NH}_3/\text{BF}_3\text{-Et}_2\text{O}$ was used. Stereoselective introduction of an azide group at C-8 was observed under appropriate conditions. Manoyl oxide **52** and 13-epimanoyl oxide **53** provided azide-ketone **54** by vinylic fragmentation with loss of C-14 and C-15.²⁵⁾

The action of $\text{NaN}_3\text{-ICl}$ or TIOAc-I_2 on labd-8(17)-en-13-ol **55** was investigated. The former reagent gave a mixture of **56** and **57**, while the latter gave a mixture of **56** and **58**.²⁶⁾



Photochemical reaction of 15,16-dinorlabd-8(17)-en-13-on **59** was investigated. Namely, UV irradiation of **59** led to the fragmentation product **60** and its photocyclization product **61**. Ethers **62** and **63** and β,γ -unsaturated alcohols **64** and **65** were formed *via* ketone **66**.²⁷⁾ A partial synthesis of methyl lambertianate **67** from 13-keto degradation product **68** of methyl agathate was reported.²⁸⁾



α - and β -Levantenolide (**34** and **35**) were synthesized using functionalization at C-12 of labdanolic diterpene as shown Chart 4.²⁹⁾

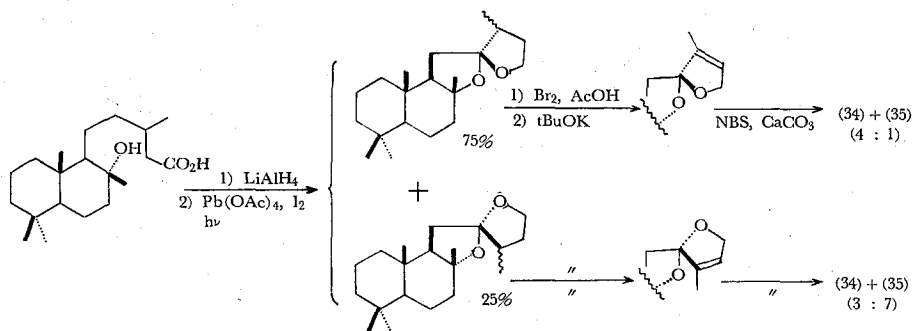


Chart 4

A synthesis of grindelic acid (69) from the easily available unsaturated (+)-ketone 66 was reported.³⁰ The sequence is shown in Chart 5.

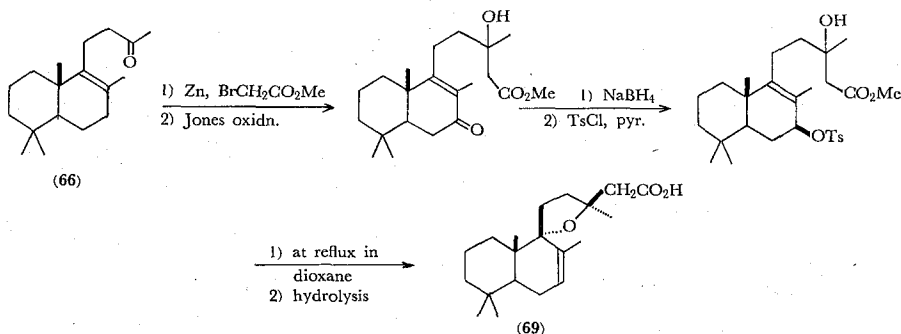


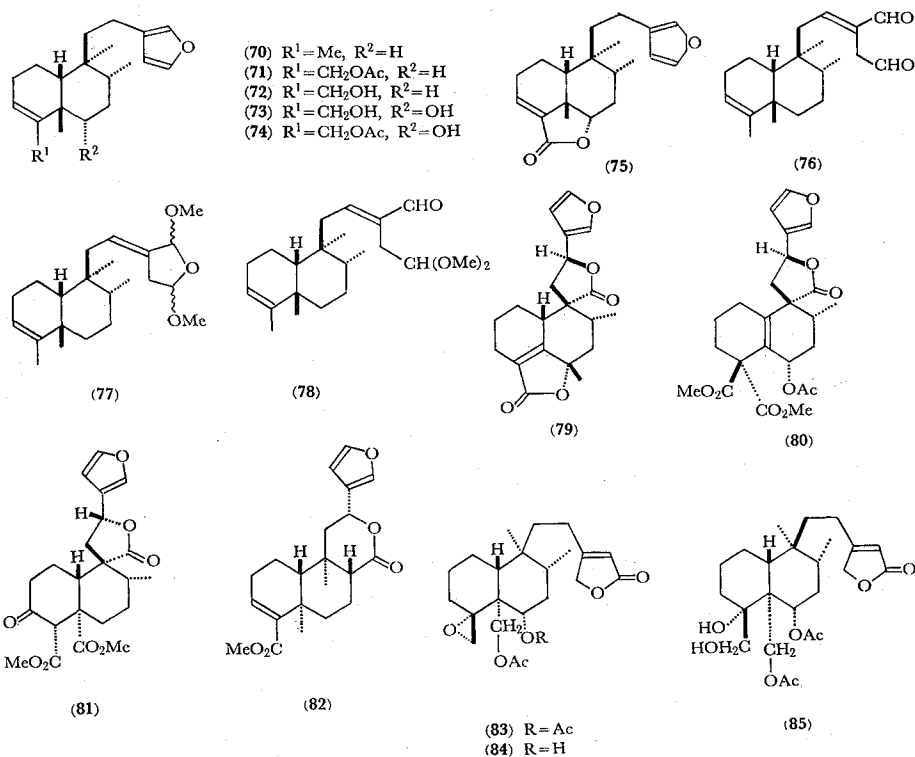
Chart 5

Isolation of labdane type diterpene from *Pinus-pumila* resin was reported,³¹ but the details are not known.

IV. CLERODANE DERIVATIVES

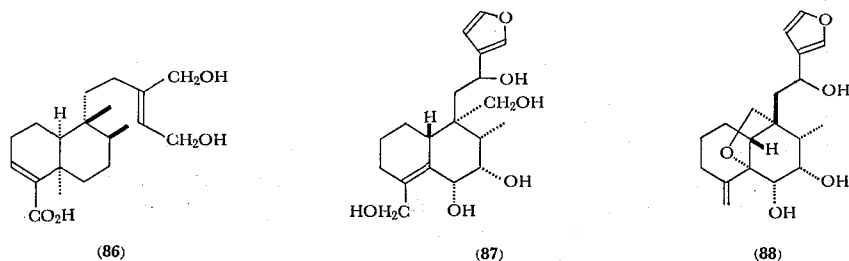
Six new diterpenoids, (70-75) were isolated from the roots of *Solidago arguta*, and their structures were deduced from their chemical and spectral properties.³² A new diterpene dialdehyde named linariidial was isolated from *Linaria japonica*, and the structure was established as 76 on the basis of the physicochemical evidence and the chemical correlation with the known furanoclerodane type compound 70. At the same time, two linariidial-analogs (77 and 78), which seem to be the artefacts formed secondarily from linariidial (76), were isolated from methanol extract of the same plant.³³ Two lactones, mallotucin A and B, were isolated from *Mallotus repandus*.³⁵ Mallotucin A was found to be identical with teucvin (79) isolated from *Teucrium viscidum* var. *Miquelianum*.³⁴ Mallotucin B (80) was found to be the first diterpenoid with geminal methoxycarbonyl groups.³⁵

The structure and stereochemistry of corylifuran, a clerodane type diterpene from *Croton corylifolius*, have been determined as 81 by chemical and spectroscopic



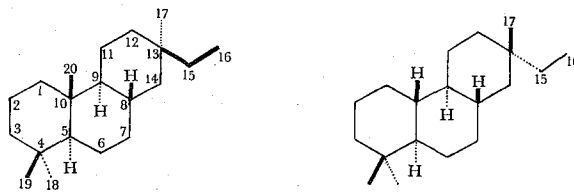
data and X-ray crystallographic analysis.³⁶⁾ Methyl barbascoate (82), a major diterpenic component of the medicinal plant *Croton californicus*, was isolated and the structure determined by a combination of spectral and X-ray crystallographic studies.³⁷⁾ The structures of Ajugarin-I, II, and III (83, 84, and 85), which are insect antifeedants, isolated from *Ajuga remota* leaves, were determined³⁸⁾

A new clerodance type diterpene, floridolic acid (86), was isolated from *Evodia floribunda* and the structure was confirmed by X-ray analysis of its methyl ester.^{39,40)} Diterpene pentol 87, obtained by reduction of teucrin A with LiAlH_4 , on treatment with 5% H_2SO_4 underwent an anisotropic rearrangement to give 88 identified by its acetates, acetonide, and oxidation products.⁴¹⁾



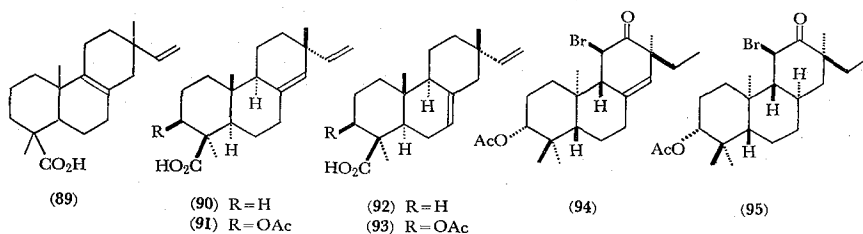
A review on the insect antifeedants found in plants was published. Several clerodane-type diterpenes were described in it.⁴²⁾

V. PIMARANE AND ISOPIMARANE DERIVATIVES

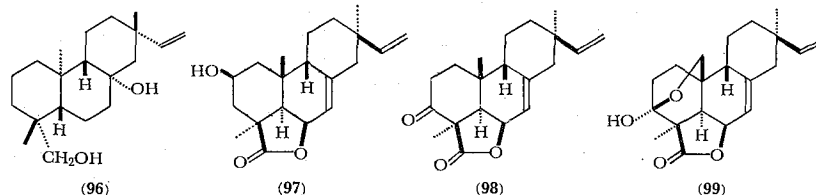


Pimarane and Isopimarane

Two diterpene acids, neothujic acid III and IV, were isolated from the fertilized female strobiles of thuja, *Thuja occidentalis*. The structure of neothujic acid III was determined as **89**.⁴³⁾ Four new pimarane type diterpene acids (**90**, **91**, **92**, and **93**) were isolated from *Dimorphotheca pluvialis*⁴⁴⁾ together with a beyerane type diterpene acid. The X-ray analyses of *ent*-3 β -acetoxy-11 α -bromoisopimar-8(14)-*en*-12-one (**94**) and its dihydroderivative (**95**) were reported.^{45,46)}

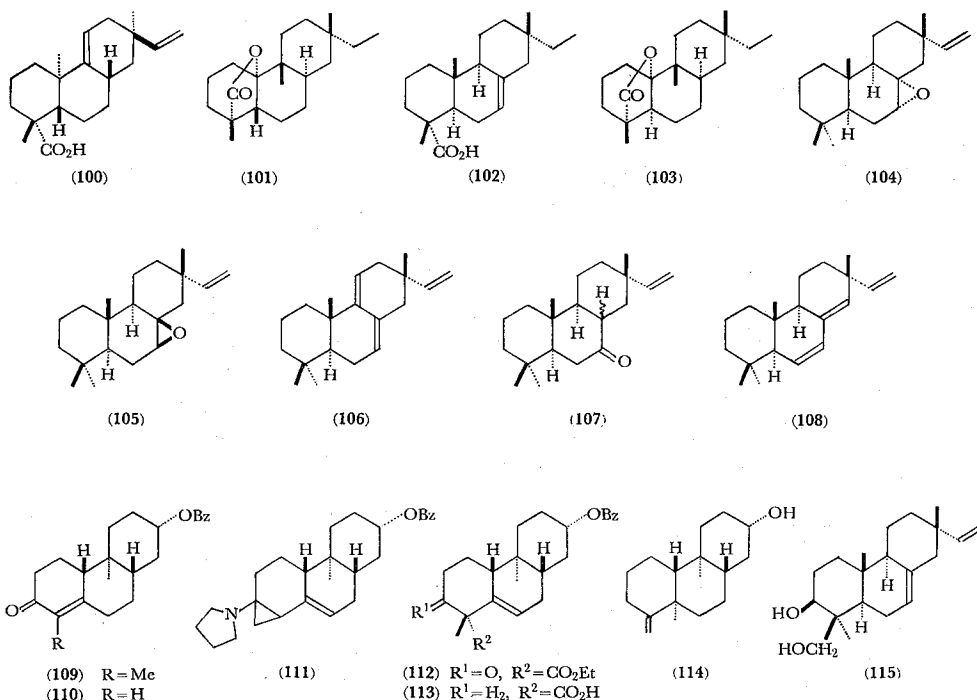


(-)-Therमारол (**96**), a new *ent*-pimarane-type diterpene diol was isolated together with *ent*-pimara-8(14), 15-dien-19-oic acid and *ent*-pimara-8(14), 15-dien-19-ol from *Jungermannia thermanum*.⁴⁷⁾ Structure **97** of momilactone-C, a minor constituent of growth inhibitors in rice husk, was determined by X-ray analysis, which revealed that C-9, C-10 linkage of **97** was unusual *cis* configuration having a boat conformation of the ring A. The stereochemistry of C-9 of previously reported momilactone-A and B has been erroneously written and should now be revised to β -configuration (**98** and **99**) with respect to hydrogen atom as in momilactone-C.⁴⁸⁾



A new pimaradiene carboxylic acid **100** was isolated from *Othonna cylindrica* as its methyl ester.⁴⁹⁾ The structure **101** for the γ -lactone derived from acid treatment of dihydroisopimaric acid (**102**) was revised to be **103** with a *cis*-A/B ring fusion, which was based on ¹³C NMR chemical shift data and spin-lattice relaxation time (T_1) measurements.⁵⁰⁾ Constitutional effects in chemical ionization mass spectrometry of di- and tri-functional isopimarane type diterpens were reported.⁵¹⁾ The acid-

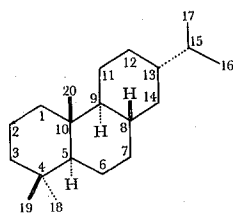
catalyzed reactions of 7α , 8α -epoxy-isopimar-15-ene (**104**) and 7β , 8β -epoxyisopimar-15-ene- (**105**) were described. The epoxides were allowed to react with boron trifluoride etherate in dry benzene to give compounds **106**, **107** and/or **108** with some miscellaneous products.⁵²⁾



An intermediate **109** in the synthesis of erythroxydiol X was prepared by methylation of **110** *via* its enamine derivative. Thus, the pyrrolidine enamine on treatment with diazomethane to give the cyclopropaphenanthrene **111** which was hydrolyzed to **109** by heating in aq. MeOH.⁵³⁾ Furthermore, alkylation of **109** with ClCO₂Et gave the ester **112** which was converted to the acid **113** by Clemmensen reduction followed by hydrolysis.⁵⁴⁾ The perhydrophenanthrenol **114** was prepared from **110** in 9 steps.⁵⁵⁾ Formulae **109-114** represent their racemate, respectively.

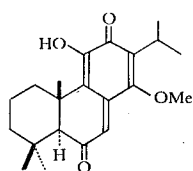
In a review on the biosynthetic studies with ¹³C labeled precursors, virescenol B (**115**) was exemplified.⁵⁶⁾

VI. ABIETANE DERIVATIVES

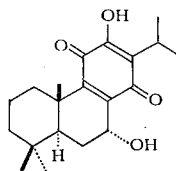


Abietane

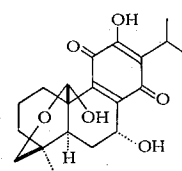
From *Hyptis fruticosa*, 14-methoxytaxodione **116** was isolated together with the known horminone **117** and its structure was determined on the basis of spectroscopic data and by chemical correlations.⁵⁷⁾ Two new diterpenoid quinones, conacytone (**118**) and icetexone (**119**) were isolated from *Salvia ballotaeflora*. Their structures were determined by the X-ray analyses.^{58,59)} The acentric crystal structure of *cis*-coleon D (**120**) was established by the X-ray analysis (by direct methods). The absolute configuration was determined from the known chirality of the A/B ring junction.⁶⁰⁾ Isolation of stemolide (**121**), a novel diterpene bisepoxide, from the leaves of *Stemodia maritima* was reported. The structure was determined by X-ray analysis.⁶¹⁾ Two alcohols isolated from *Nepeta granatensis* were identified as 7 α , 18-dihydroxy-14-abietene and 14 α , 18-dihydroxy-7-abietene by their chemical reaction.⁶²⁾



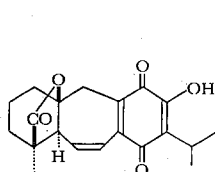
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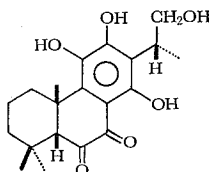
(117)



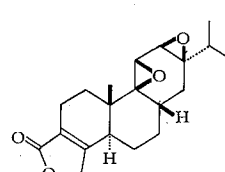
(118)



(119)

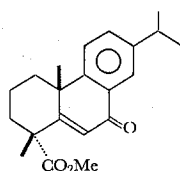


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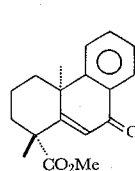


(121)

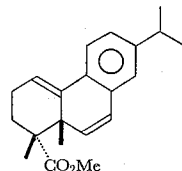
Kinetics of the thermal isomerization of abietic acid in the presence of air at 200° into palustric and neoabietic acid was investigated.⁶³⁾ Iodine catalyzed disproportionation of abietic acid gave dihydroabietates or dehydroabietates. E.s.r. meas-



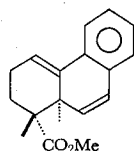
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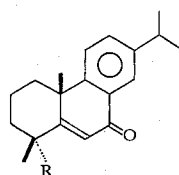
(123)



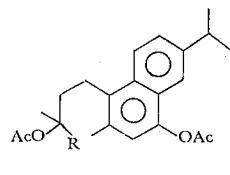
(124)



(125)



(126) R=Me

(127) R=CH₂OAc

(128) R=Me

(129) R=CH₂OAc

urements suggested the intermediacy of free radicals.⁶⁴⁾ Acid treatment in acetic anhydride of blocked cyclohexadienone derivatives **122** and **123** gave **124** and **125**, respectively, through Wagner-Meerwein rearrangement of the angular methyl group. On the other hand, under similar conditions, **126** and **127** were transformed into **128** and **129**, respectively, as the result of an abnormal dienone phenol rearrangement.⁶⁵⁾

Direct introduction of bromine into the ring A of phenacylidene derivatives of *l*-abietic acid was developed and it was applied to the conversion of abietic acid into teideadiol (**130**) having a hydroxy group on the ring A of its abietane skeleton.⁶⁶⁾ (Chart 6)

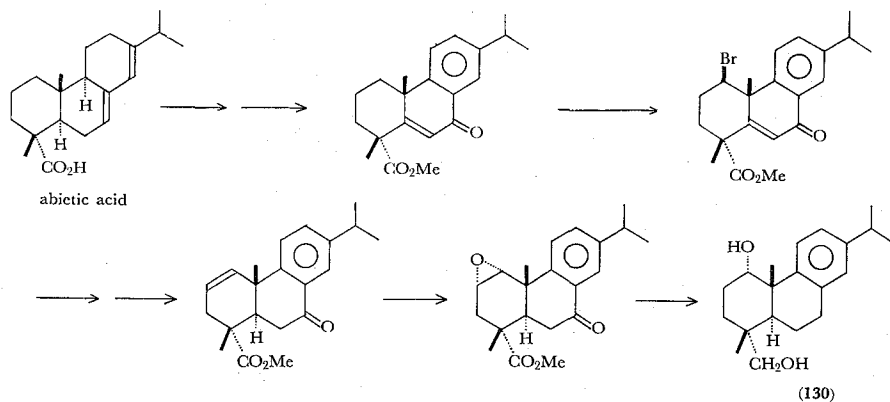
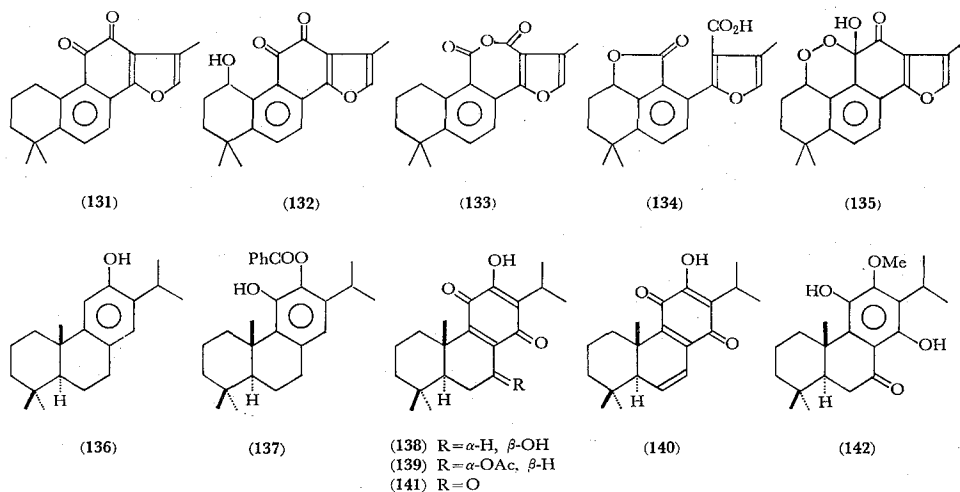


Photo-oxidation of tanshinone II (**131**) was published. Thus, UV irradiation of **131** in the presence of air afforded 9-hydroxy-tanshinone (**132**), anhydride **133**, and lactone **134**. The formation of these compounds was explained in terms of an intermediate **135**, derived from tanshinone II by photoenolization and oxygenation.⁶⁷⁾

Oxidation of ferruginol **136** with benzoyl peroxide gave 12-benzoyloxy-11-hydroxyabieta-8, 11, 13-triene (**137**) which was converted into taxoquinone (**138**), 7 α -acetoxyroyleanone (**139**), dehydroroyleanone (**140**), horminone (**117**), 7-oxoroyle-



leanone (141), and inuroyleanone (142).⁶⁸⁾

Transformation of dehydroabietic acid (**145**) to a key intermediate for the synthesis of steroids was examined. 13-Isopropyl-18, 19-bisnor-5 β -podocarpa-8, 11, 13-trien-3-one (**143**) was synthesized from **145** *via* the ketone **144**.⁶⁹⁾ In addition, methyl 14-oxo-podocarp-18-oate **146** was synthesized from **122**.⁷⁰⁾

A potential synthetic intermediate **147** of *rac*-carnosic acid **148** was synthesized as shown in Chart 7.⁷¹⁾

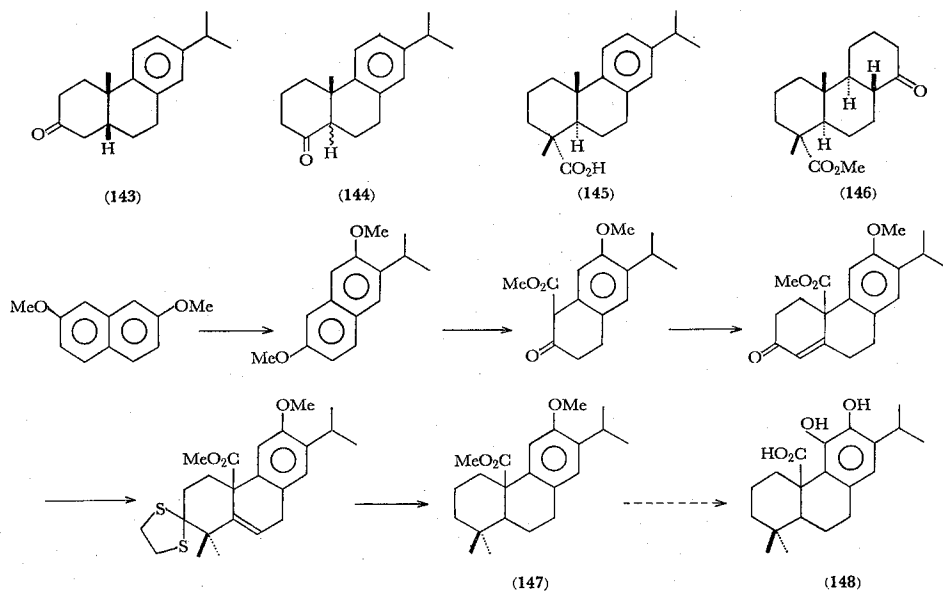


Chart 7

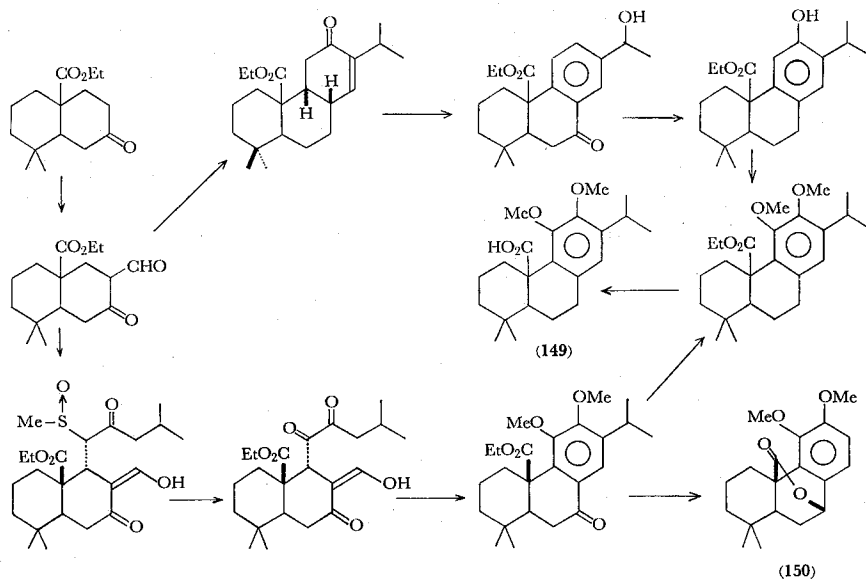
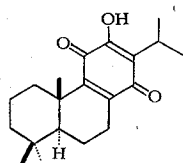


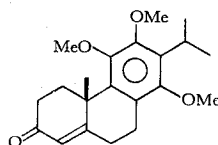
Chart 8

The total syntheses of *rac*-carnosic acid dimethyl ether (149) and *rac*-carnosol dimethyl ether (150) were achieved.⁷²⁾ The outline is shown in Chart 8.

rac-Royleanone (151) was prepared in 16 steps from 2,3,6-trimethoxybenzoic acid *via* the trimethoxy intermediate 152.⁷³⁾



(151)



(152)

A short and highly stereoselective total synthesis of *rac*-callitrisic acid (153) was described.⁷⁴⁾ The sequence is shown in Chart 9.

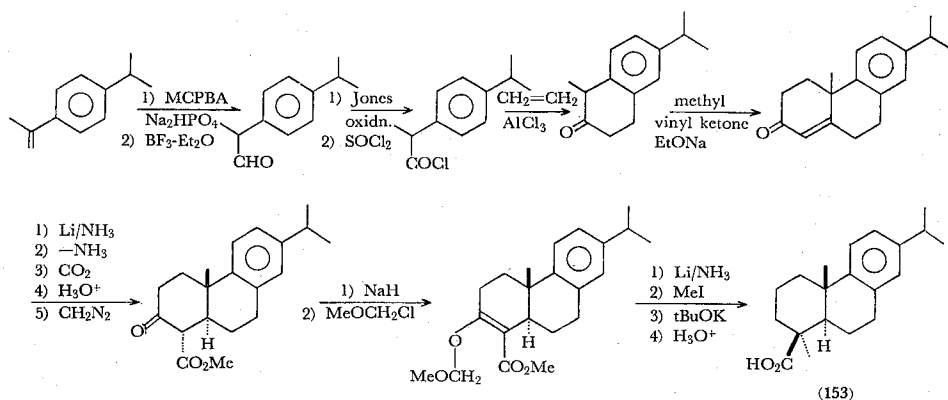


Chart 9

Stereoselective isopropyl-methyl migration in *l*-abietic acid derivative was investigated, and was applied to synthesis of 15-beyerene (*l*-hibaene) (154) from *l*-abietic acid as shown in Chart 10.⁷⁵⁾

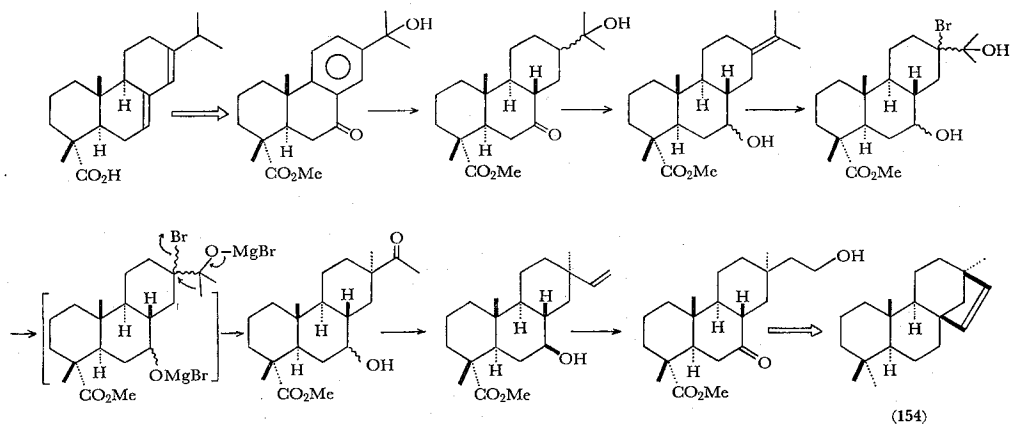
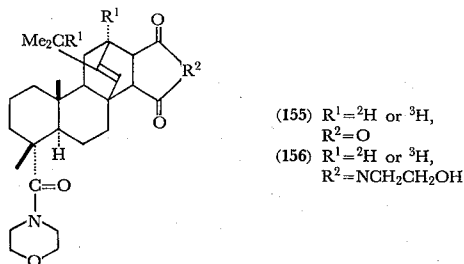


Chart 10

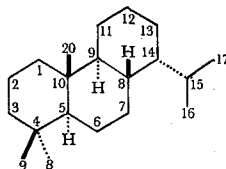
Synthesis of deuterium and tritium labeled derivatives (155 and 156) of moleo-pimaric acid was reported.⁷⁶⁾



Effects of hydrofluorene and hydrophenanthrene compounds derived from dehydroabietic acid (145) on the second leaf sheath growth of rice seedlings were examined in the presence and absence of gibberellic acid.⁷⁷⁾

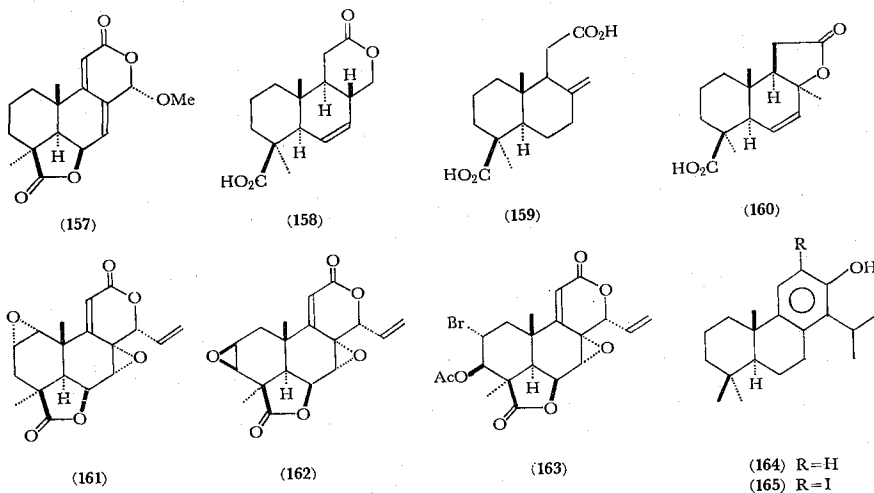
A review on the synthetic chemistry starting from abietic acid was published.⁷⁸⁾

VII. TOTARANE DERIVATIVES



Totarane

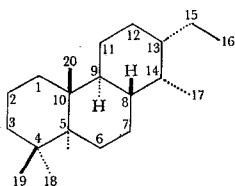
Three new C_{16} terpenoids, which may lie on the biosynthetic pathway for the antifungal metabolite LL-Z 1271 α (157), were isolated from an *Acrostalagmus* fungus, and assigned the structures 158, 159, and 160.⁷⁹⁾ The compound 157 has been assumed to be derived from diterpene biogenetically.⁸⁰⁾



The previously published structure **161** of sellowin B was revised to **162** on the basis of the X-ray crystallographic study of its bromohydrin acetate **163**.⁸¹⁾ Treatment of **164** with thallium (I) acetate and iodine gave **165**.⁸⁾

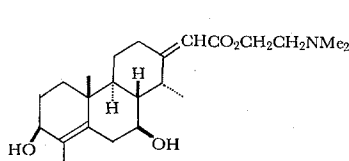
The chemistry of biologically active norditerpene dilactones isolated from *Podocarpus* species was discussed.⁸²⁾

VIII. CASSANE DERIVATIVES

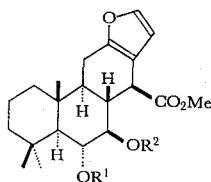


Cassane

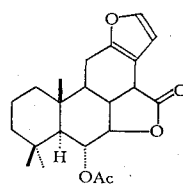
19-Nor-4-dehydrocassaidine (**166**) was isolated from the bark of *Erythrophloeum coumunga* and its structure was determined by spectral data.⁸³⁾ Investigation of diterpenoids in four species of *Pterodon* was carried out. From *P. pubescens*, the new ester **167** was isolated. From *P. emarginatus*, compounds **168**, **169**, **170**, and **171** were isolated. The diterpenoids **169** and **170** were isolated also from *P. polygalaeiflorus*. The compound **170** was further isolated from *P. apparicioi*.⁸⁴⁾



(166)

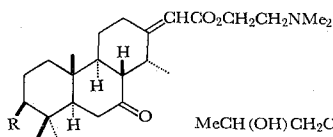


(167) $R^1 = R^2 = \text{Ac}$
 (169) $R^1 = R^2 = \text{H}$
 (170) $R^1 = \text{Ac}$, $R^2 = \text{H}$
 (171) $R^1 = \text{H}$, $R^2 = \text{Ac}$



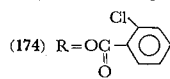
(168)

From cassaine (**172**), several analogs, (**173-179**) were prepared. From 3-dehydrocassaic acid (**180**), derivatives **181** and **182** were made.⁸⁵⁾



(172) $R = \text{OH}$

(173) $R = \text{OCOCH2CH2Cl}$

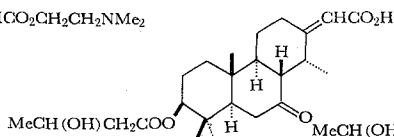


(174) $R = \text{OCOC(=O)C6H4Cl}$

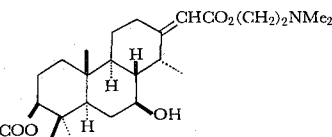
(175) $R = \text{OCOCH=CHMe}$

(176) $R = \text{OCOCH2COMe}$

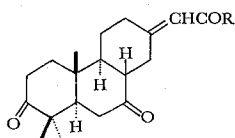
(177) $R = \text{OCOCH2CH(OH)Me}$



(178)

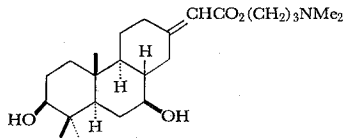


(179)

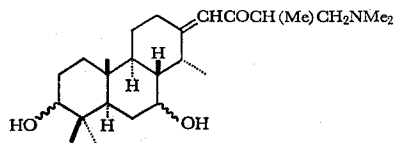


(180) $R = \text{OH}$

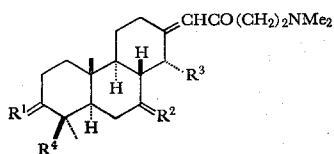
(182) $R = \text{NHCH2CH2NMe2}$



(181)



(183)

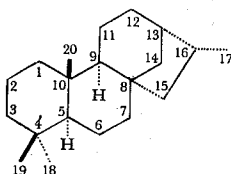


(184) $R^1=O$, $R^2=H_2$, $R^3=H$, $R^4=Me$

(185) $R^1=H_2$, $R^2=O$, $R^3=Me$, $R^4=CO_2Me$

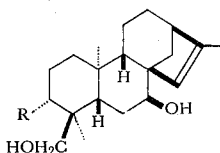
Compounds 183, 184, and 185 were prepared from the known derivatives of cassenic acid, and 183 and 185 were shown to have cardiotonic activity.⁸⁶⁾

IX. KAURANE DERIVATIVES



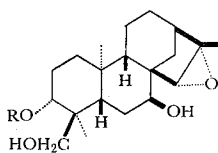
Kaurane

From *Sideritis paulii*, sideridiol (186), isofoliol (187), and a new diterpene, epoxyisofoliol (188) were isolated.⁸⁷⁾ A new diterpenoid, epoxyisolidol (189) was isolated from *Sideritis biflora*.⁸⁸⁾ Four new hydroxylated *ent*-kauran-19-oic acids, 190, 191, 192, and 193 were isolated from *Eupatorium album*.⁸⁹⁾



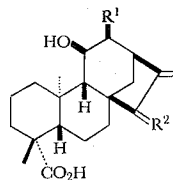
(186) $R=H$

(187) $R=OH$



(188) $R=H$

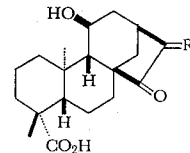
(189) $R=Ac$



(190) $R^1=H$, $R^2=\alpha-H$, $\beta-OH$

(191) $R^1=H$, $R^2=O$

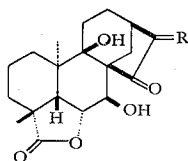
(192) $R^1=OH$, $R^2=\alpha-H$, $\beta-OH$



(193) $R=\alpha-H$, $\beta-Me$

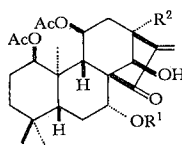
(194) $R=\alpha-Me$, $\beta-H$

From *Pteris dispar*, 191 and four new diterpenes, 193, 194, 195, and 196 were isolated.⁹⁰⁾ Eight new diterpenes, rastronols A (197), B (198), C (199), D (200), E (201), F (202), G (203), and H (204), were isolated from *Englerstrum scandens*.⁹¹⁾



(195) $R=CH_2$

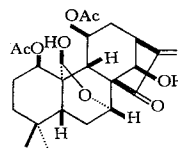
(196) $R=\alpha-H$, $\beta-Me$



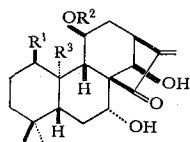
(197) $R^1=R^2=H$

(198) $R^1=H$, $R^2=OH$

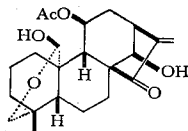
(199) $R^1=Ac$, $R^2=OH$



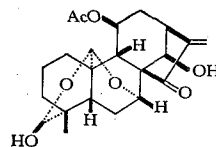
(200)



- (201) $R^1=OH$, $R^2=H$,
 $R^3=CHO$
 (202) $R^1=H$, $R^2=Ac$,
 $R^3=CH_2OH$



(203)

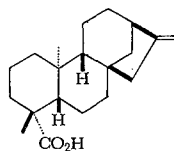


(204)

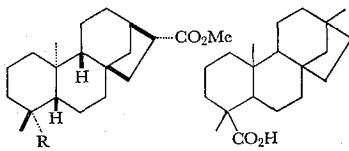
ent-Kaur-16-en-19-oic acid (205) was isolated as its methyl ester from *Othonna cylindrica*.⁴⁹⁾ The root bark of *Annona senegalensis* is used by Nigerian herbalists to treat cancer. From the root bark of this plant, six crystalline materials were isolated. They were found to be *ent*-kauran-16 β -ol, *ent*-kaur-16-en-19-oic acid (205), methyl *ent*-16 α -kauran-19-al-17-oate (206), methyl *ent*-19-nor-16 α -kauran-4 β -ol-17-oate (207), compound 208, and 209 or 210.⁹²⁾

The root and overground part of *Verbesina angustifolia* were found to contain diterpenic acids 205 and 211. The root of *V. oncophora* also contained these two acids and *ent*-kauran-13-ol.⁹³⁾

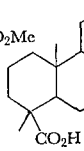
A new diterpenic acid 212 was isolated from *Melampodium perfoliatum*.⁹⁴⁾ The "coffee atractylosides" 213 and 214 were isolated from *Coffea arabica*.⁹⁵⁾



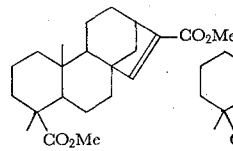
(205)



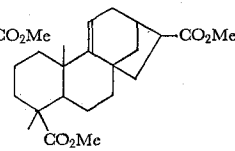
- (206) $R=CHO$
 (207) $R=OH$



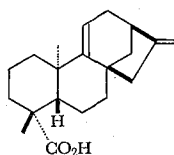
(208)



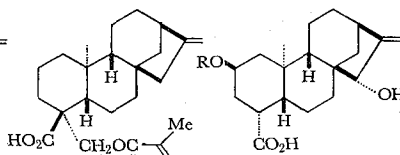
(209)



(210)

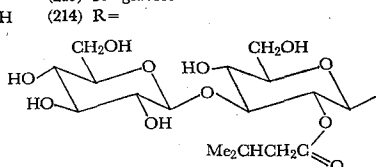


(211)

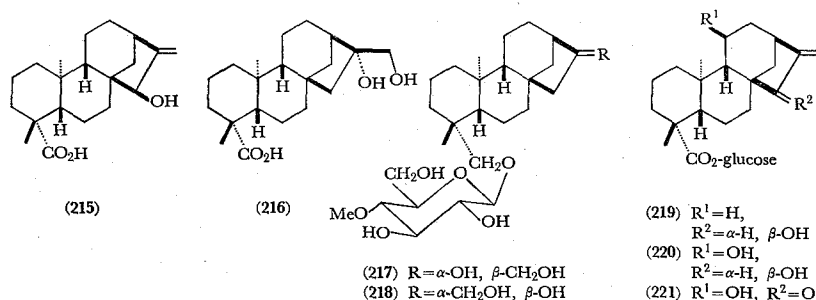


(212)

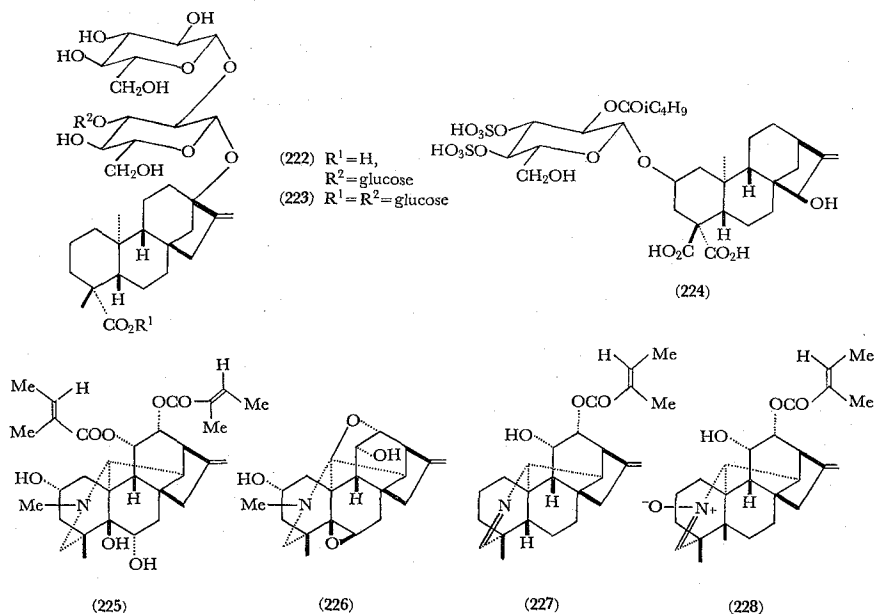
- (213) $R=$ glucose
 (214) $R=$



The enzymatic hydrolysis of the glycosides fraction of the leaves of *Stevia paniculata* gave four aglycones and their structures were elucidated as 190, 191, 215, and 216.⁹⁶⁾ Two new diterpene-glycosides, microlepin and 16-epimicrolepin, were isolated from the overground part of *Microlepis marginata* and assigned the structures 217 and 218.⁹⁷⁾ The structures of paniculosides, I, II, and III, three new diterpene-glycosides of *Stevia paniculata*, were determined as 219, 220, and 221.⁹⁸⁾



From the leaves of *Stevia rebaudiana*, two new sweet glucosides, rebaudiosides A and B, were isolated besides the known glucosides, stevioside and steviolbioside. On the basis of IR, MS, ¹H and ¹³C NMR as well as chemical evidence, the structures 222 and 223 were assigned to rebaudiosides A and B, respectively.⁹⁹⁾ Isolation and identification of the hypoglycemic agent, carboxyatractylate (224), from *Xanthium strumarium* were reported.¹⁰⁰⁾



Anopterine was isolated from the leaf and bark of *Anopterus macleayanus* and bark of *A. glandulosus*, and its structure was determined to be represented as 225. Hydrolysis of anopterine and oxidation with potassium ferricyanide gave an unusual product 226, whose structure was confirmed by the X-ray analysis.^{101,102)} To two new minor alkaloids of *A. macleayanus*, anopterimine and anopterimine N-oxide, were assigned the structures 227 and 228, and the partial structures of two other new alkaloids, hydroxyanopterine and dihydroxyanopterine were also reported.¹⁰³⁾

The structures of grayanotoxins XVI and XVII, two physiologically active diterpenoids of *Leucothoe grayana*, were elucidated as 229 and 230.¹⁰⁴⁾ On the basis of the

results of an X-ray analysis the stereochemistry of pieristoxin G (231) was discussed.¹⁰⁵⁾

The ¹³C NMR spectra of some kauranoid diterpenes have been assigned. The application of the results to the determination of the sites of hydroxylation in this series was discussed.¹⁰⁶⁾ The X-ray analyses of 232¹⁰⁷⁾ and 233¹⁰⁸⁾ were reported. The reaction of the keto esters 234 and 235 with Na in liquid ammonia afforded mixtures of *ent*-kaurane, *ent*-beyerane, and dimeric products.¹⁰⁹⁾

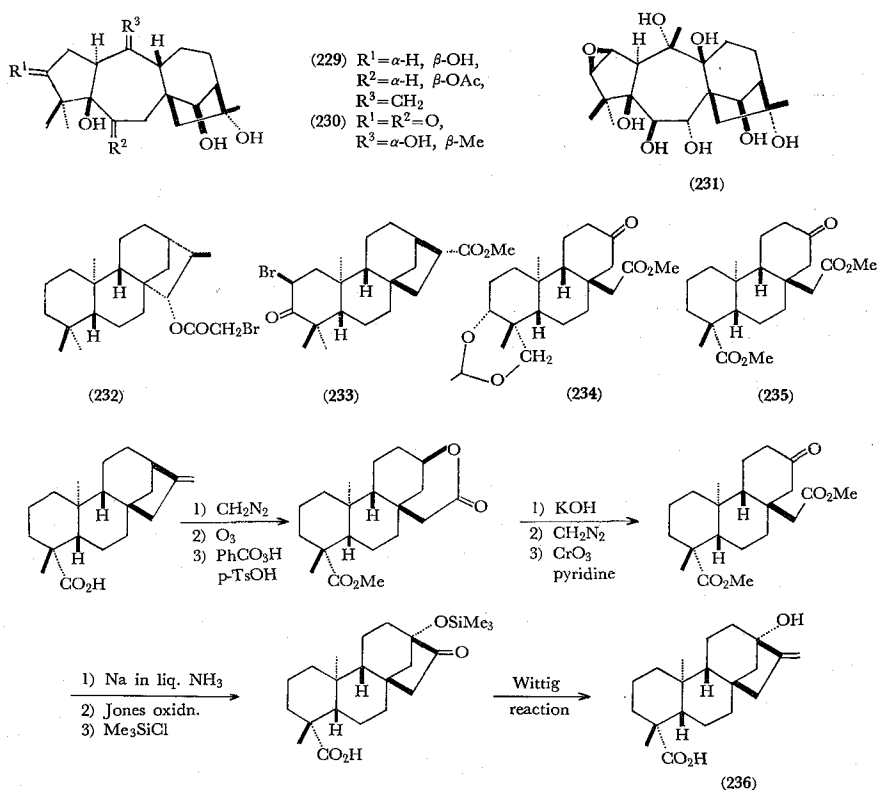
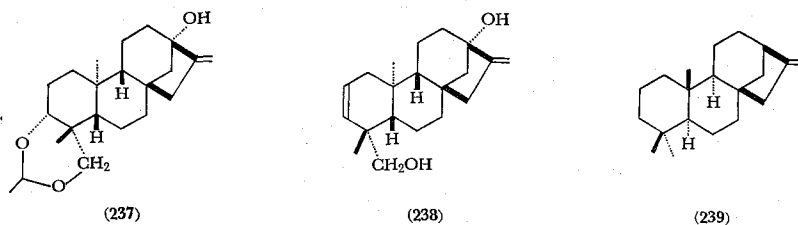
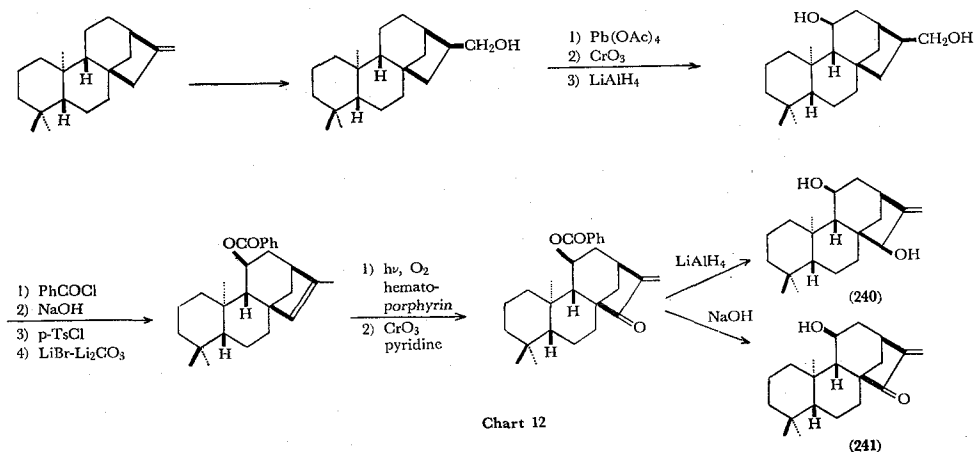


Chart 11

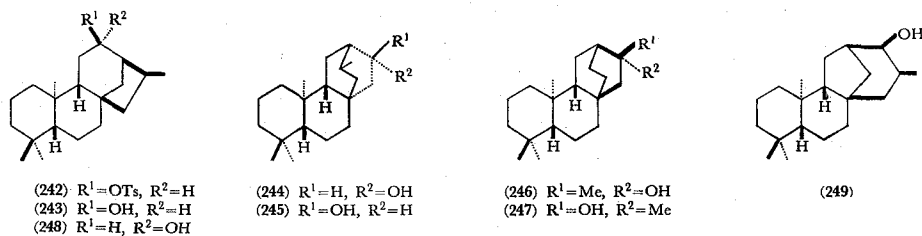
The synthesis of steviol (236) (Chart 11) and two A-ring modified analogs 237 and 238 was reported.¹¹⁰⁾



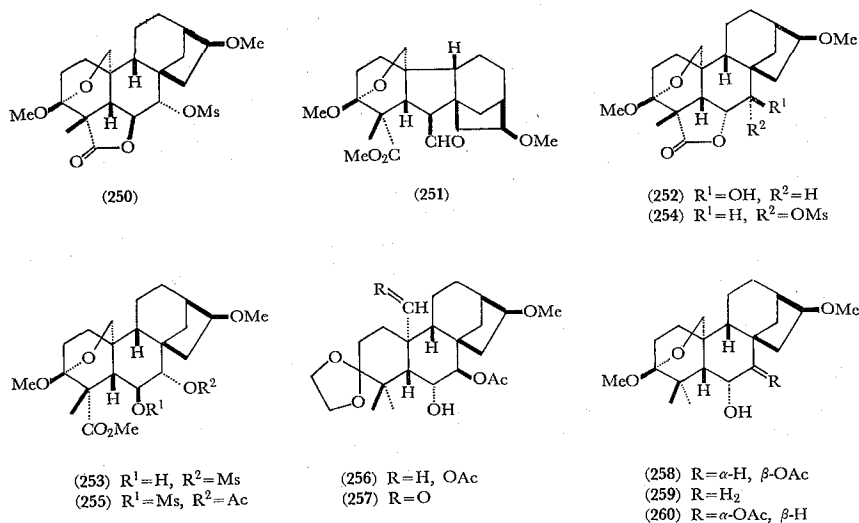
The full details of the synthesis of phyllocladene (239) from abietic acid was published.¹¹¹⁾ The synthesis of *ent*-kaur-16-ene-11 α , 15 α -diol (240) and *ent*-kaur-16-en-15-on-11 α -ol (241) from *ent*-kaur-16-ene was performed. The outline is shown in Chart 12.¹¹²⁾



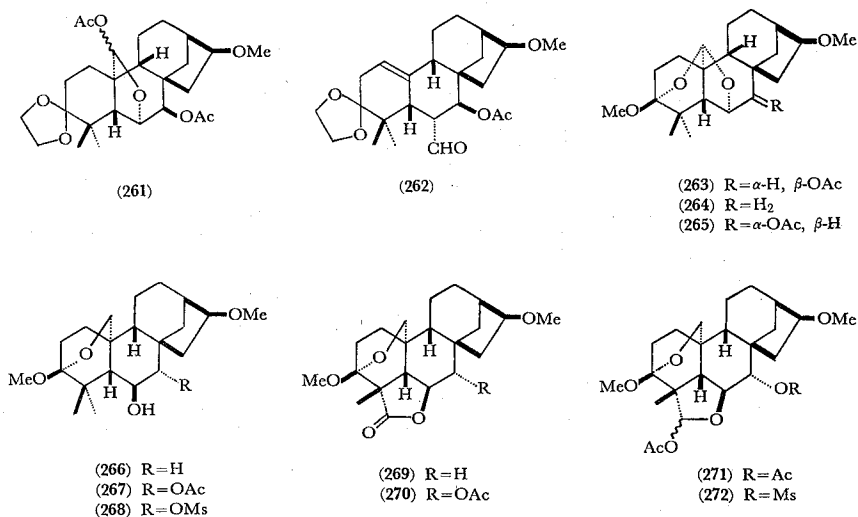
Buffered formolysis of *ent*-12 α -*p*-tolylsulfonyloxykaurane (242) followed by hydrolysis gave chiefly the corresponding alcohol 243, smaller amounts of the epimeric *ent*-atisan-13- (244 and 245) and 16-ols (246 and 247), together with traces of *ent*-kauran-12 β -ol (248) and the *ent*-14(13 $\rightarrow$ 12)*abeo*-kauran-13 α -ol (249).¹¹³⁾



The detailed investigation on the ring B contraction of kauranolides and related compounds into gibberellane-type compounds was carried out. The lactone 250

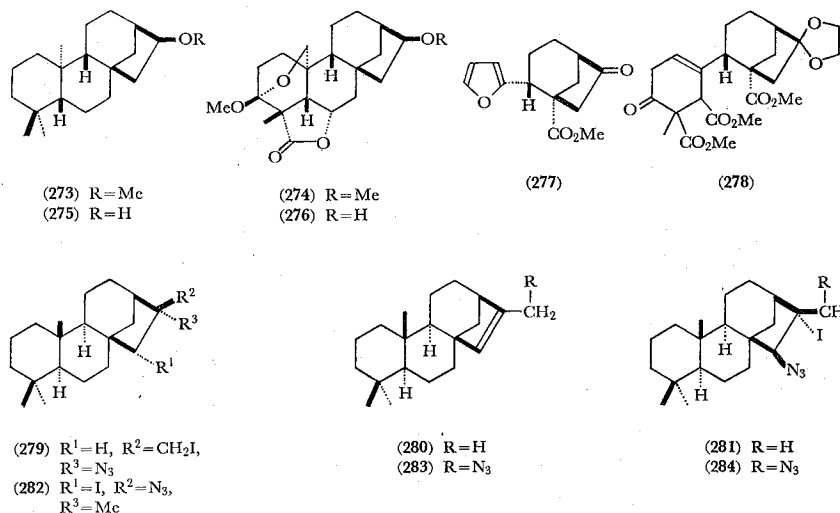


on treatment with base and subsequent methylation gave the gibberellane aldehyde **251** and the alcohol **252**. The ester **253** gave a similar result. The lactone **254** on the same treatment afforded only the desired product **251** quantitatively. The ring B contraction did not proceed with the ester **255**. The results are rationalized in terms of stereochemical considerations.¹¹⁴⁾



On the hypiodite reaction, 17-norkauran-6 α -ols **256**, **257**, **258**, **259**, and **260** gave **261**, **262**, **263**, **264**, and **265**, respectively. 17-Norkauran-6 β -ols **266**, **267**, and **268** on the same reaction yielded **269**, a mixture of **270** and **271**, and **272**, respectively. Thus, the O-functionalization of the inactive C-19 methyl group of 17-norkauran-6-ols was achieved.¹¹⁵⁾

Treatment of *ent*-16 α -methoxy-17-norkaurane (**273**) and lactone **274** with boron

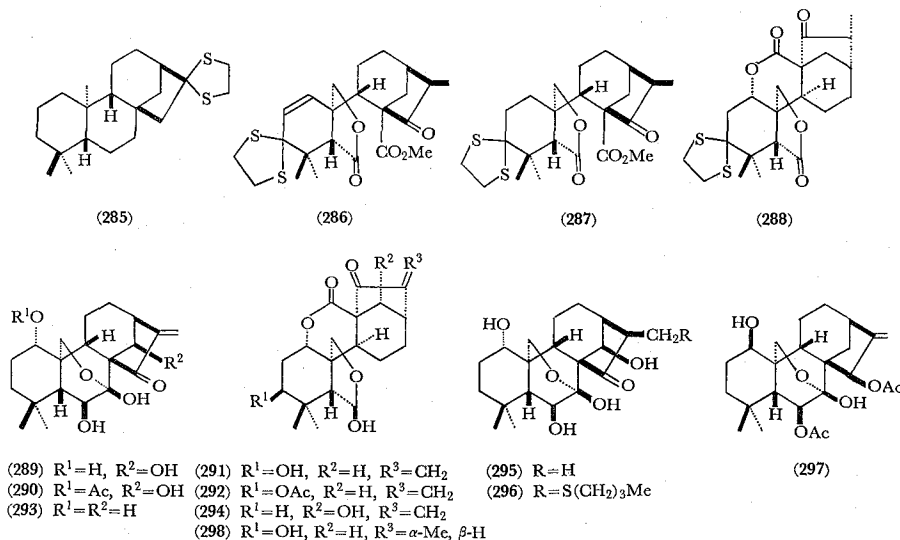


trifluoride-ether complex in ethanedithiol gave the corresponding alcohols **275** and **276**, respectively, with retention of the original stereochemistry.¹¹⁶⁾ Demethylfujenoic acid derivative **278** was synthesized from the key intermediate **277**.¹¹⁷⁾

Reaction of sodium azide and iodine chloride with phyllocladene (**239**) gave the compound **279**. On the same treatment, isophyllocladene (**280**) gave two major products, **281** and **282**, and two minor products, **283** and **284**.²⁶⁾

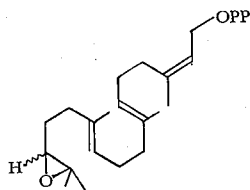
Thioacetals **285-288** were dethioacetalized by the treatment with thallium (III) nitrate under mild conditions for a short time to recover the parent carbonyl compounds in good yields. The reaction mechanisms were also discussed.¹¹⁸⁾

Oridonin (**289**), lasiokaurin (**290**), enmein (**291**), enmein-3-acetate (**292**), and related compounds (**293** and **294**), all of which have α -methylene cyclopentanone function in their molecule, were shown to have antitumor activity against Ehrlich ascites carcinoma inoculated into mice and specific activity against gram-positive bacteria. On the other hand, compounds **295** and **296**, trichokaurin (**297**), and dihydroenmein (**298**) showed any activity neither against tumor nor against bacteria. Thus it was concluded that the α -methylene-cyclopentanone system must be an important active center. Biomimetic reactions of oridonin and enmein with several thiols *etc.* supported this conclusion.^{119,120)}

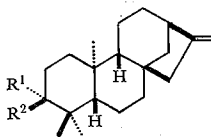


Enzymatic cyclization of *rac*-14,15-oxidogeranylgeranyl pyrophosphate (**299**) to hydroxykaurenes **300** and **301** was reported.¹²¹⁾ Conversion of geranylgeranyl pyrophosphate to *ent*-kaurene in enzyme extracts of sonicated chloroplasts was reported.¹²²⁾ Incorporations of *ent*-kaur-16-ene and *ent*-kaur-16-en-15-one (**302**) into enmein (**291**) and oridonin (**289**) by *Isodon japonicus* were demonstrated by tracer experiments with seven labeled *ent*-kaurene derivatives. Furthermore, evidence was obtained that functionalization of *ent*-kaur-16-ene at the allylic C-15 atom proceeds through direct oxygenation.¹²³⁾

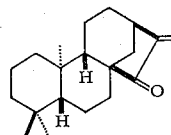
ent-Kaur-16-en-19-oic acid (**205**) was transferred by *Cunninghamella blakesleeana*



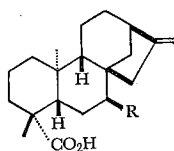
(299)



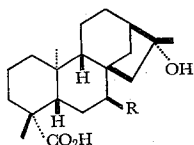
(300) $R^1=OH, R^2=H$
(301) $R^1=H, R^2=OH$



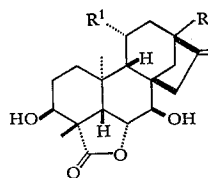
(302)



(205) $R=H$
(303) $R=OH$



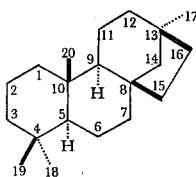
(304) $R=H$
(305) $R=OH$



(306) $R^1=R^2=H$
(307) $R^1=OH, R^2=H$
(308) $R^1=H, R^2=OH$

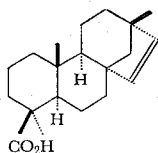
to a series of hydroxylated derivatives, 216, 303, 204, and 305.¹²⁴⁾ Hydroxylation of 3 β , 7 β -dihydroxykaurenolide (306) by *Rhizopus arrhizus* afforded 307 and 308.¹²⁵⁾

X. BEYERANE DERIVATIVES

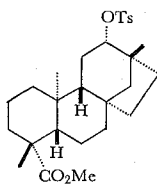


Beyerane

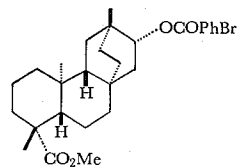
A new beyerane type diterpenic acid 309 accompanied by some new pimaran type diterpenes was isolated from *Dimorphotheca pluvialis*.⁴⁴⁾ The X-ray analysis of methyl



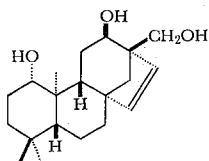
(309)



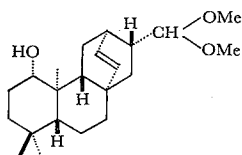
(310)



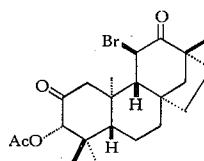
(311)



(312)



(313)

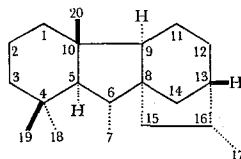


(314)

ent-16 β -*p*-bromobenzyloxy-17(16 $\rightarrow$ 12)*abeo*-atisan-19-oate (**311**), a derivative of a formolysis product of methyl *ent*-12 β -toluene-*p*-sulfonyloxybeyeran-19-oate (**310**), was reported.¹²⁶⁾

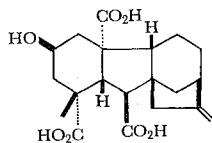
A minor product in the reaction of jativatriol (**312**) with hydrochloric acid was elucidated as **313** by the X-ray analysis.¹²⁷⁾ The X-ray analysis of *ent*-3 β -acetoxy-11 α -bromobeyer-2, 12-dione (**314**) was reported.¹²⁸⁾

XI. GIBBERELLANE DERIVATIVES

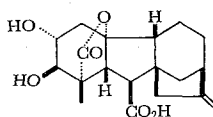


Gibberellane

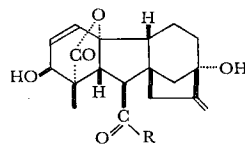
A general method for the conversion of 3-hydroxygibberellins into the methyl esters of 2-hydroxygibberellins was published. Thus the structures of two new gibberellins, GA₄₆ (**315**) from seed of *Echinocystis macrocarpa* and GA₄₇ (**316**) from cultures of *Gibberella fujikuroi* (strain GF-1a), were determined by these partial syntheses.¹²⁹⁾



(315)



(316)



(317) R = O-N

(318) R = NH-CH₂C₆H₅

(319) R = O-NH-CO(CH₂)₂CONHCH₂C₆H₅

The ¹³C-NMR study of several gibberellin derivatives was reported.¹³⁰⁾ The aminolysis of gibberellin-A₃-(N-hydroxy-succinimide)-ester (**317**) with benzylamine

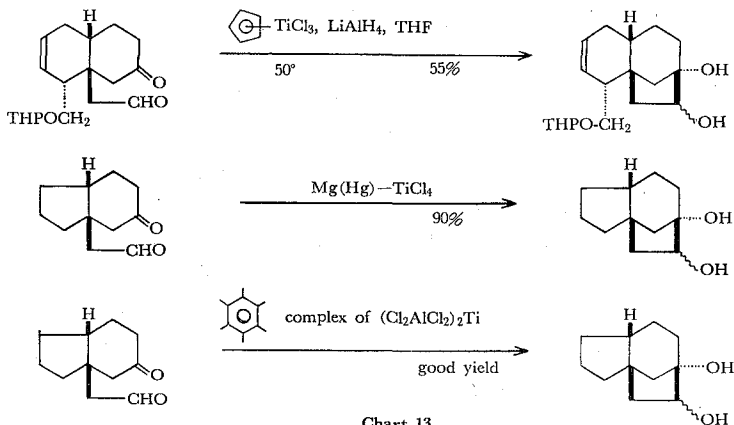
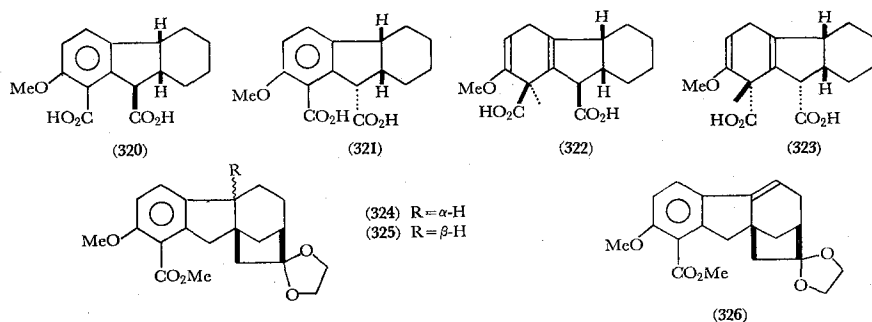


Chart 13

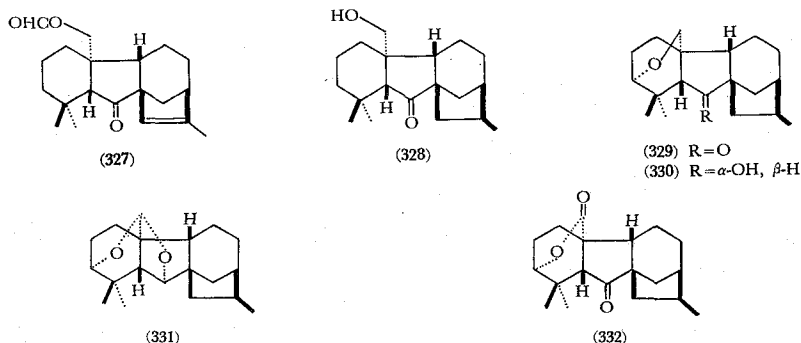
yielded gibberellin-A₃-benzylamide (**318**) and O-(gibberellin-A₃-oyl)-N-(benzylamino)-succinoyl-hydroxy-amine (**319**).¹³¹⁾ Three types of new reagents for the intramolecular pinacolic coupling of dicarbonyl compounds were developed. These are magnesium amalgam-titanium tetrachloride, cyclopentadienyltitanium trichloride-lithium aluminum hydride, and the hexamethylbenzene complex of the well-defined Ti (II) species (Cl₂AlCl₂)₂Ti.¹³²⁾ These new pinacolic coupling reactions seem to be very effective for the construction of C-D ring system in synthesis of A₃-type gibberellins. (Chart 13)

A new stereocontrolled synthesis of some intermediates **11a** and **11b** for C₂₀ gibberellins were published.⁵⁾ The reductive methylation of each epimeric diacid **320** and **321** was investigated by successive reaction with lithium in THF-liquid ammonia followed by methyl iodide. In each case, the diacid product (**322** from **320** and **323** from **321**) was formed by introduction of the C-4 methyl group from the side of the molecule opposite to the carboxyl group at C-6.¹³³⁾



Various methods for the introduction of a carboxyl group into the benzylic position of compounds, **324**, **325**, and **326** were investigated. Among them, the best was found to involve deprotonation of these acetal esters with lithium N-cyclohexyl-N-t-butylamide, followed by carboxylation, which was highly stereoselective.¹³⁴⁾

The hypiodite reactions on the 7-norgibberellane derivatives were studied. The reaction with 7-nor-6-on-20-ol **328** derived from compound **327** afforded a high yield of 3,20-ether **329**. The second hypiodite reaction with the α-ol **330** performed between C-6 and C-20 and yielded compound **331**, whose oxidation with the Jones reagent gave ketolactone **332**.¹¹⁵⁾



Ring B contraction of kauranoids and related compounds into gibberellane-type compounds was investigated in detail.¹¹⁴⁾ (See section IX.)

A formal total synthesis of *rac*-gibberellin A₁₂ (**340**) mimicking the biogenetical pattern was achieved by employing methyl *rac*-7,16-dioxo-17-norkauran-19-oate (**337**) as a relay compound.^{135,136)} The outline is shown in Chart 14. Thus, compound **333** was converted into **337** via 7-en-13-ol **334**, 7-keto-13-al **335**, and a key intermediate **336** for ring D closure. Conversion of **337** into diketolactone **338** had been done.¹³⁷⁾ Then the 16-oxo compound **338** was transformed into the 16-ene **339**, whose conversion into GA₁₂ (**340**) had been performed.^{137,138)}

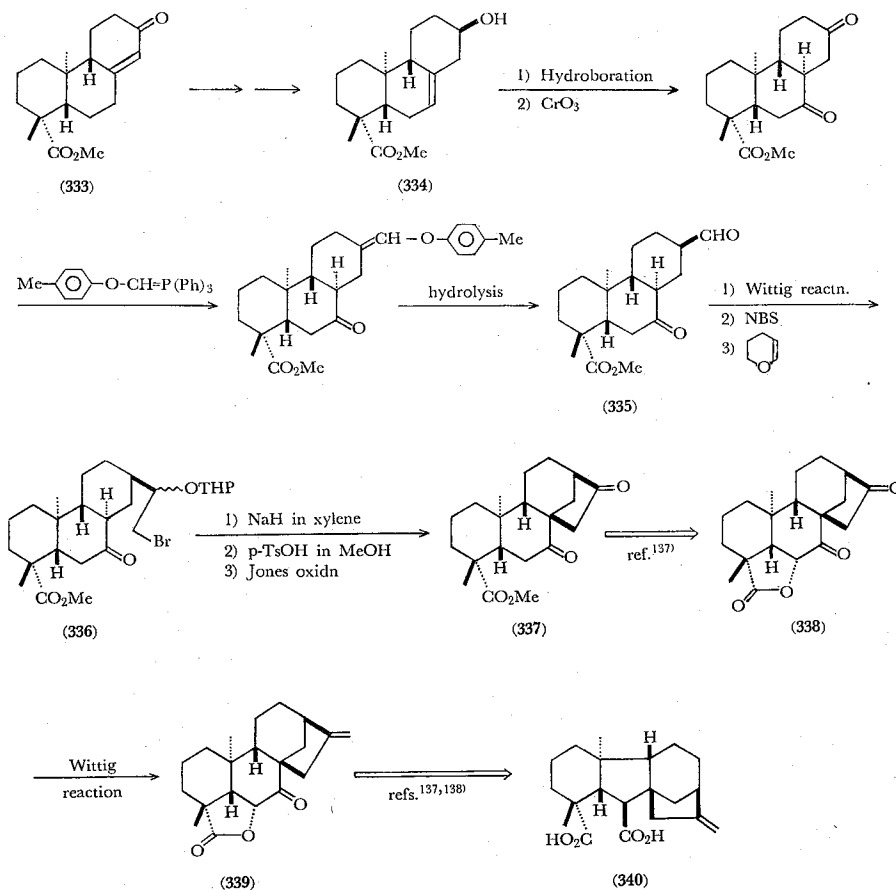
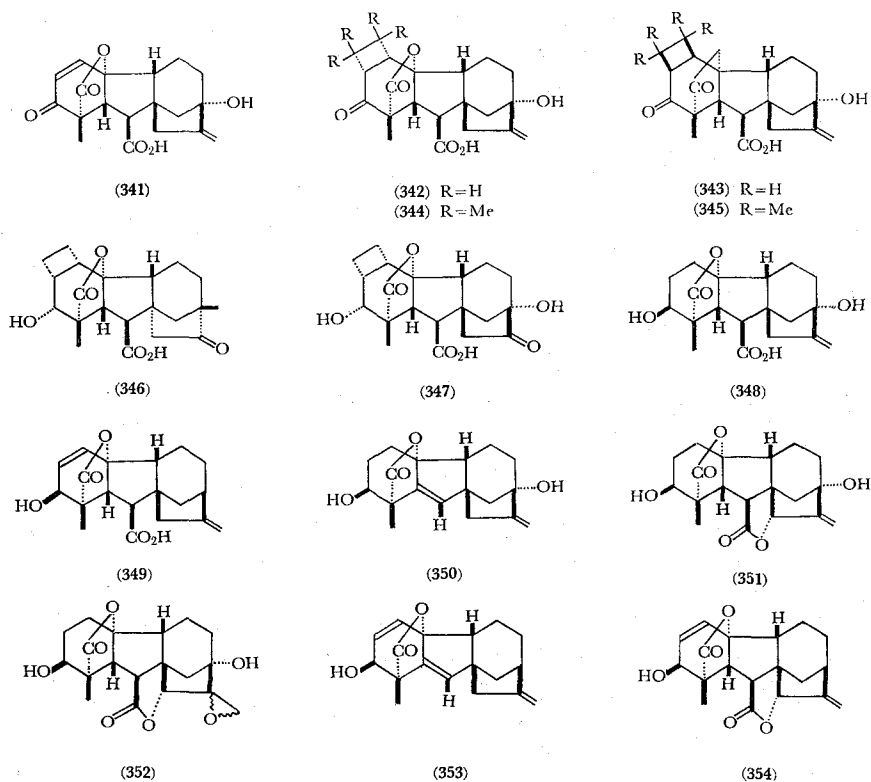


Chart 14

The photochemical [2+2]-cycloaddition of ethylene and tetramethylethylene to 3-dehydrogibberellin A₃ (**341**) under $n \rightarrow \pi^*$ -excitation conditions was investigated. The reaction lead to a 3:1 ratio of the *cis*-fused α - and β -cyclobutane annelated epimers **342** and **343** as well as **344** and **345** in 70 and 86% yield, respectively. Reduction of the annelated products with NaBH₄ was also discussed.¹³⁹⁾

The structure and molecular packing of the cyclobutane annelated pseudogibberellin A₁ derivative **346**, prepared by trifluoroacetic acid catalyzed Wagner-Meer-

Chemistry on Diterpenoids in 1976



wein rearrangement of **347**, was established by X-ray analysis.¹⁴⁰⁾ The oxidative lactonization and oxidative decarboxylation of gibberellin A₁ (**348**) and A₇ (**349**) with neutral manganese dioxide were investigated. The reaction with GA₁ gave compounds, **350**, **351**, and **352** and that with GA₇ produced **353** and **354**.¹⁴¹⁾

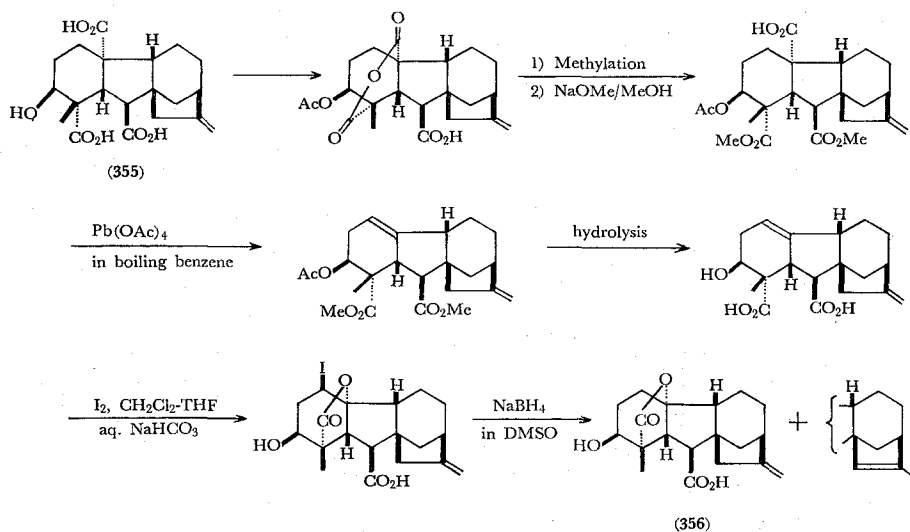
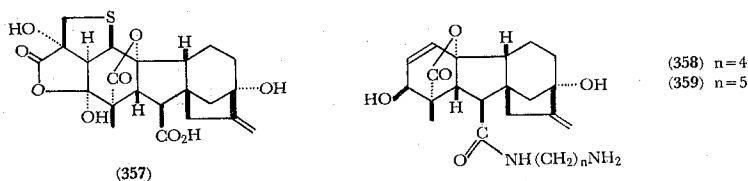


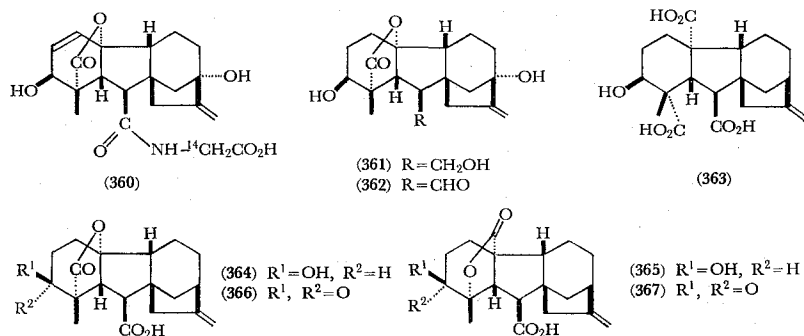
Chart 15

The synthesis of 2, 3-(^3H)-GA₉ with a specific activity of 47 Ci mmole⁻¹ was reported.¹⁴²⁾ The chemical conversion of GA₁₃ (355) into GA₄ (356) was accomplished.¹⁴³⁾ The route is shown in Chart 15.

The synthesis of gibberethione (357) isolated from seed of *Pharbitis nil* as a catabolic product of GA₃ was carried out by the direct coupling of 3-dehydro-GA₃ (341) and mercaptopyruvic acid.¹⁴⁴⁾ The uniformly ^3H -labeled gibberellic acid (GA₃) amides, 358 and 359, were prepared by amidation of the mixed anhydride of uniformly ^3H -labeled GA₃ and inactive GA₃ with H₂N(CH₂)_nNH₂ (n=4 and 5).¹⁴⁵⁾

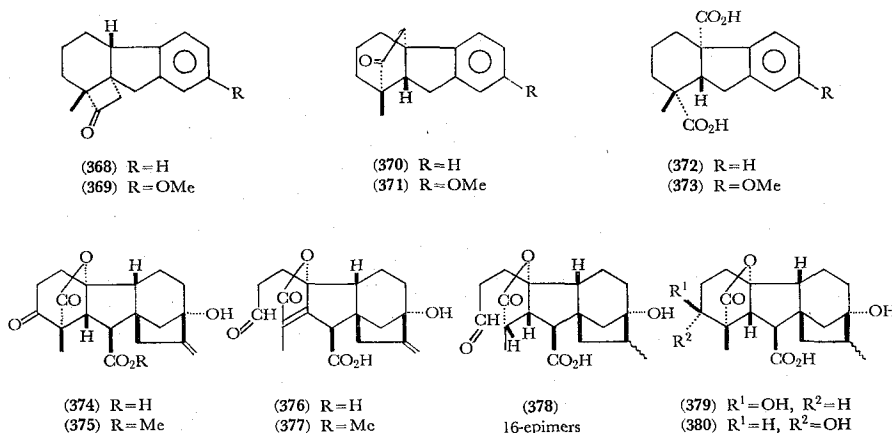


The synthesis of neutral and amino-substituted amides of the gibberellin A₃ and A₁ series *via* aminolysis of the corresponding gibberellin carboxylic acid anhydrides was published. The mass spectra and ^1H -NMR data of these compounds are also discussed.¹⁴⁶⁾ The synthesis of gibberellin-A₃-oyl-2- ^{14}C -glycine (360) was reported.¹⁴⁷⁾ Gibberellin A₁-(7)-alcohol (361) and gibberellin-A₁-(7)-aldehyde (362) were prepared from GA₁ (348).¹⁴⁸⁾



GA₁₃ (363), on treatment with Pb(OAc)₄-dimethylformamide (DMF) at 18°C, afforded a mixture (60:40) of the known GA₄ (364), identified by g.l.c.-mass spectrometry of the methyl ester, and the new isomeric lactone 365; minor amounts of the corresponding 3-ketones 366 and 367 were also formed. This is the first chemical correlation of C₂₀ gibberellin to C₁₉ gibberellin.¹⁴⁹⁾ A rearrangement of compounds 368 and 369 with triethyloxonium fluoroborate in CH₂Cl₂ into the corresponding bridged ketones 370 and 371 was published. Their transformation to some key hydrofluorene synthons 372 and 373 towards the C₂₀ gibberellins was also reported.¹⁵⁰⁾

The photolysis of 3-dehydro-gibberellin A₁ (374) followed by methylation gave 4⁴-3.4-secoaldehyde 377 *via* acid 376. The initial methylation of 374 followed by photolysis also gave 377. The tetrahydro-compound 378 derived from 376 was treat-



ed with alkali to yield epimeric alcohols **379** and **380**.¹⁵¹⁾ Thus, this reaction should be a good evidence for the retro-aldol mechanism to epimerization of the 3-hydroxy-group of GA₁ under the basic condition.

A formal synthesis of gibberellin A₁₂ (**340**) was accomplished starting from *l*-abietic acid.¹⁵²⁾ The synthetic route is summarized in Chart 16.

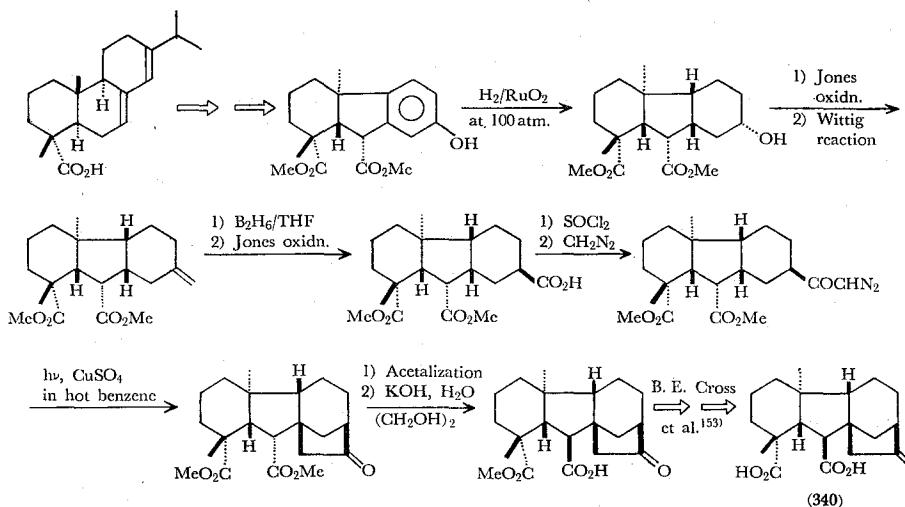
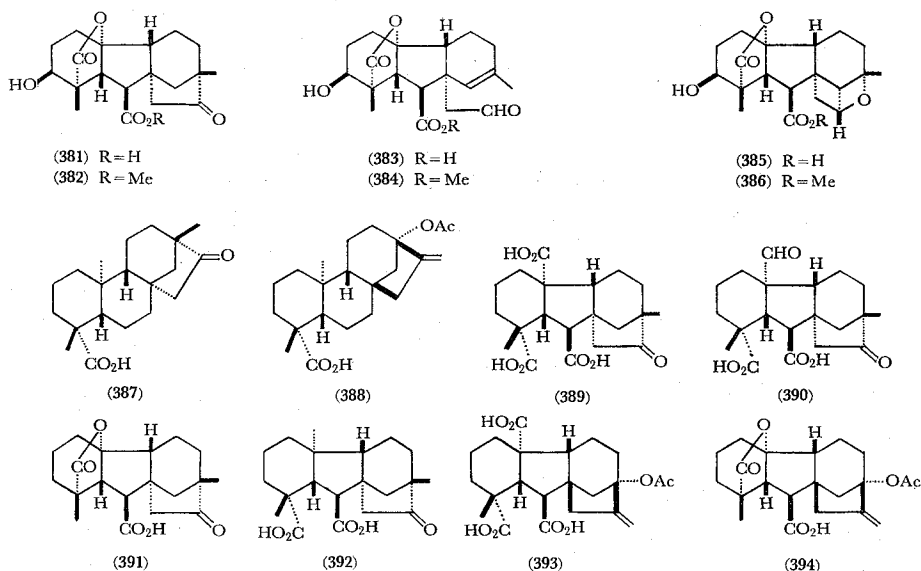


Chart 16

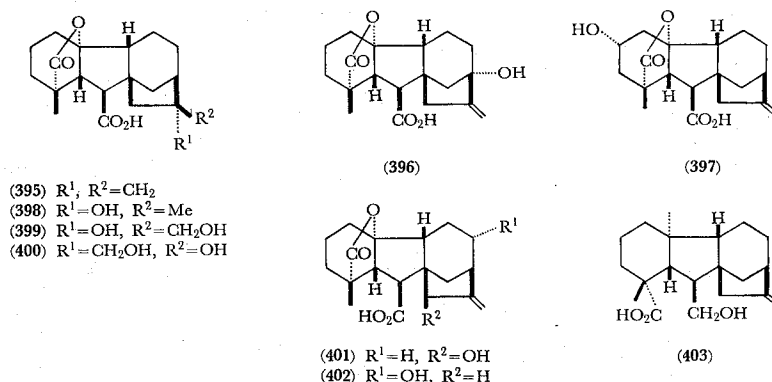
The $n \rightarrow \pi^*$ photolysis of gibberellin C (**381**) and its methyl ester (**382**) was performed by Norrish I cleavage to form secoaldehydes **383** and **384**, respectively. The subsequent intramolecular [2+2] cycloaddition of these secoaldehydes gave oxetane products **385** and **386**.¹⁵⁴⁾

Isosteviol (**387**) and steviol acetate (**388**) were efficiently metabolized by cultures of resuspended mycelium of *Gibberella fujikuroi*, mutant B1-41a. Isosteviol was exclusively converted into ring-CD-rearranged derivatives (**389-392**) of gibberellins A₁₇, A₁₉, A₂₀, and 13-hydroxygibberellin A₁₂. Steviol acetate was mainly trans-



formed into the 7β -hydroxy- and $6\beta, 7\beta$ -dihydroxy-derivatives and to the 13-acetates (393 and 394) of gibberellins A_{17} and A_{20} .¹⁵⁵⁾

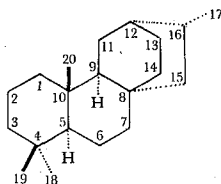
Microbiological hydroxylation of gibberellin A_9 (395) and its methyl ester was investigated employing *Gibberella fujikuroi*, mutant B1-41a. Gibberellin A_9 was principally metabolized into gibberellins A_{20} (396) and A_{40} (397). Other metabolites were detected by g.l.c.-mass spectrometry. Gibberellin A_9 was partially metabolized by cultures of *Rhizopus nigricans* to give only gibberellin A_{10} (398). Gibberellin A_9 methyl ester, however, was converted into the methyl esters of the 16α - and 16β -epimers (399 and 400) of 16, 17-dihydro-16, 17-dihydroxygibberellin A_9 , GA_{20} (396), GA_{40} (397), GA_{45} (401), and a monohydroxygibberellin A_9 (possibly 402).¹⁵⁶⁾



Origin of the oxygen atoms in the lactone bridge of C_{19} -gibberellins was studied. [^{18}O]-Label in the 19-oic acid of the C_{20} gibberellins, GA_{12} (340) and GA_{12} -alcohol (403), was incorporated without loss into C_{19} -gibberellins by cultures of *Gibberella fujikuroi*, mutant B1-41a.¹⁵⁷⁾ Biological activities of fluorogibberellins and interactions with unsubstituted gibberellins were examined.¹⁵⁸⁾ A Japanese review,

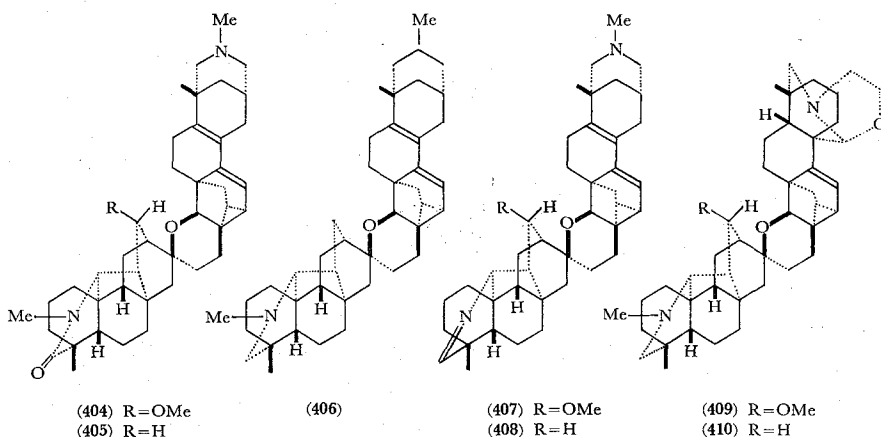
whose title is "Recent advances of biosynthetic study of gibberellins", was published.¹⁵⁹⁾ In a Japanese review on the inhibitors against isoprenoids biosyntheses, a biosynthetic route of gibberellin A₃ was briefly illustrated.¹⁶⁰⁾ A review "Studies on gibberellins in higher plants" was published in Japanese.¹⁶¹⁾

XII. ATISANE DERIVATIVES

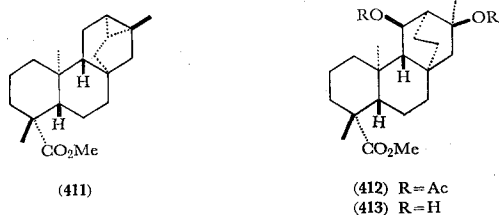


Atisane

The structures of staphigine (404) and staphirine (405), two novel bisditerpene alkaloids from *Delphinium staphisagria*, were established utilizing ¹³C and ¹H NMR spectroscopy.¹⁶²⁾ The structure elucidation of three novel alkaloids from *D. staphisagria*, staphidine (406), staphinine (407), and staphimine (408), was accomplished.¹⁶³⁾ Staphisagnine (409) and staphisagrine (410), two new bis-diterpene alkaloids, were isolated from the mother liquors of the same plant.¹⁶⁴⁾



The molecular structure of a minor product of oxidative cleavage of methyl *ent*-trachyloban-19-oate (411) with thallic acetate was determined as 412 by the X-ray analysis of the corresponding diol 413.¹⁶⁵⁾



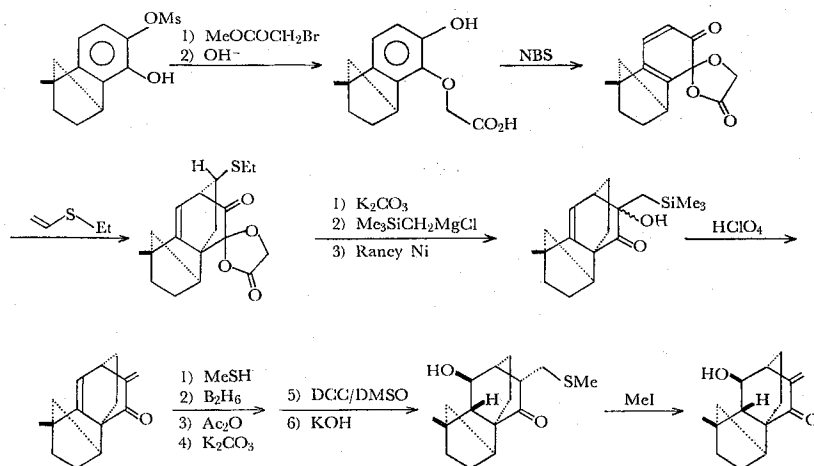
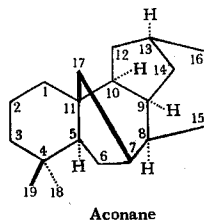


Chart 17

The construction of the substituted denudatine system by diene addition was reported.¹⁶⁶⁾ The outline is shown in Chart 17.

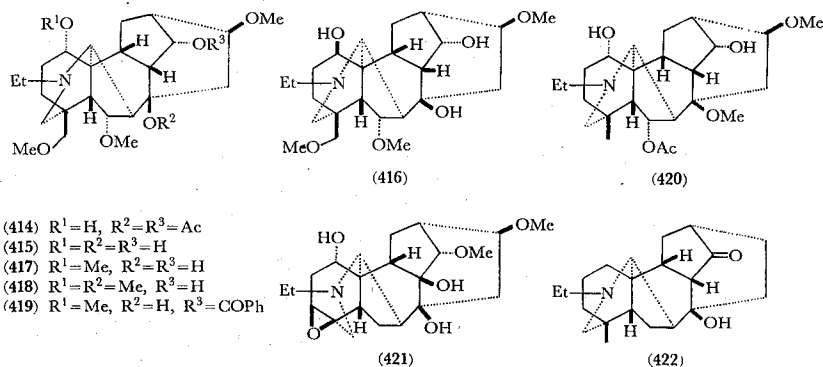
Two papers which were interesting for synthesis of atisane type diterpene alkaloids were published.^{6,7)}

XIII. ACONANE DERIVATIVES



Aconane

A new alkaloid, delphisine (414) was isolated from *Delphinium staphisagria*. Neoline (415) was prepared from delphisine (414) by several routes. Thus, 1α -hydroxy group of neoline was supported, and the revised structure 416 assigned by Marion



*et al.*¹⁶⁷⁾ was proved to be in error. On the basis of other well-established chemical correlations, the structures of chasmanine and homochasmanine must also be revised to **417** and **418**, respectively.¹⁶⁸⁾ Furthermore, the structure of chasmanine was established by an X-ray analysis of chasmanine 14 α -benzoate (**419**) hydrochloride.¹⁶⁹⁾

A new alkaloid whose structure was elucidated as **416** was isolated from the same plant source.¹⁷⁰⁾ Structure **420** was assigned to alkaloid A isolated from *Delphinium bicolor* by the examination of its ¹³C NMR spectrum.¹⁷¹⁾ The structure and absolute configuration of excelsine (**421**) was determined by an X-ray analysis of its hydroiodide.¹⁷²⁾ The X-ray analysis of the compound **422** which was synthesized from atisine was reported.¹⁷³⁾

An important intermediate **423** for the total synthesis of chasmanine (**417**) was synthesized as shown in Chart 18.¹⁷⁴⁾

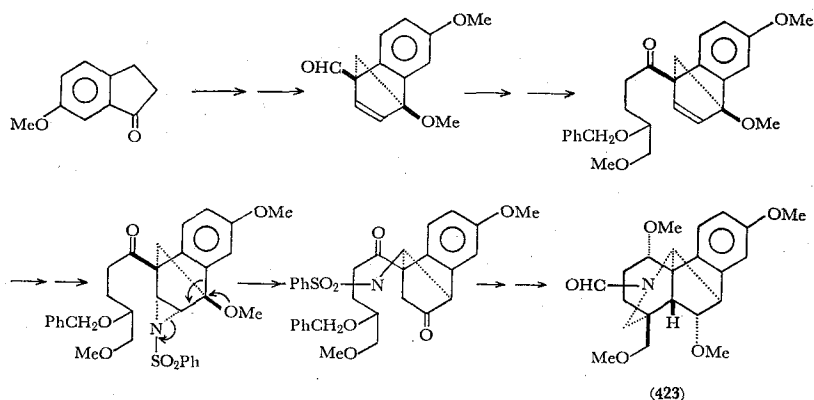
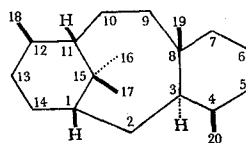


Chart 18

In a review article titled "the diterpenoid alkaloids of *Delphinium staphisagria*" was described the chemistry of aconane type alkaloids together with other alkaloids.¹⁷⁵⁾

XIV. TAXANE DERIVATIVES

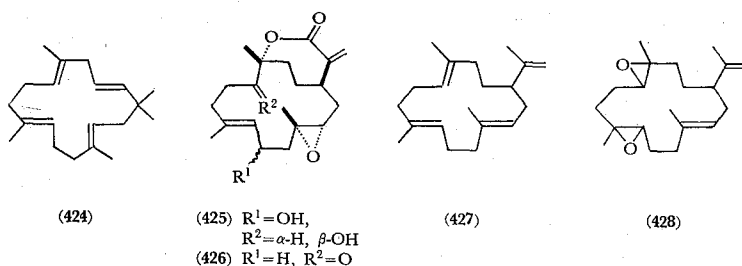


Taxane

No papers have been published on the title topics in 1976.

XV. THE OTHERS

New diterpenes, flexibilene (**424**),¹⁷⁶⁾ 6-hydroxysinulariolide (**425**), 11-dehydro-sinulariolide (**426**), (E)-(-)-cembrene A (**427**), and 3,4:11,12-diepoxyembrene A (**428**) were isolated from the soft coral, *Sinularia flexibiles*, as the minor diterpenoids.¹⁷⁷⁾



Duva-4, 8, 13-triene-1, 3-diol (429) found in the leaf wax of *Nicotiana tobacum* was shown to have highest concentration in the wax from young leaves and quantitatively decrease in importance with leaf age.¹⁷⁸⁾ Absolute stereochemistry of mukulol (430) was determined by chemical correlation with cembrene A (427) and (+)-*cis*-piperitol (431).¹⁷⁹⁾

The biogenetic type cyclization of geranylgeranic acid chlorid (432) followed by a series of reactions *via* *rac*-mukulol (430) afforded *rac*-cembrene (433).¹⁸⁰⁾ *rac*-Incensole (434) was also synthesized from *rac*-mukulol (430).¹⁸¹⁾ A total synthesis of casbene (436) from methyl *rac*-*cis*-chrysanthemate (435) was accomplished.¹⁸²⁾ The outline is shown in Chart 19.

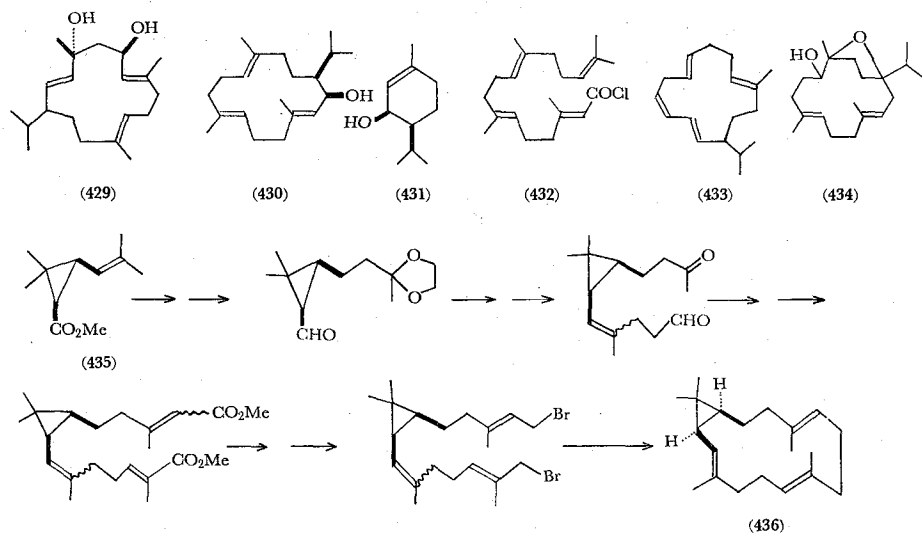
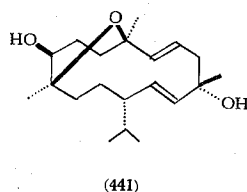
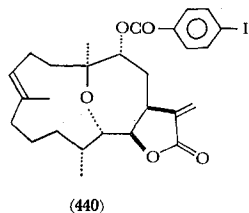
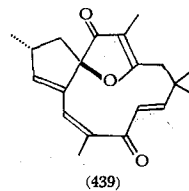
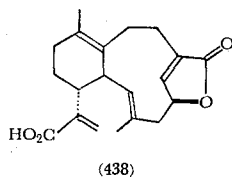
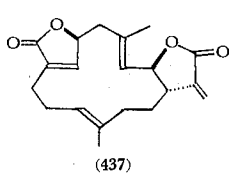


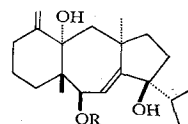
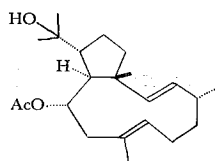
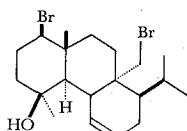
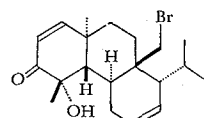
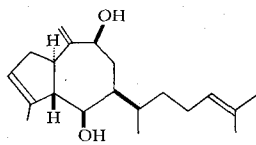
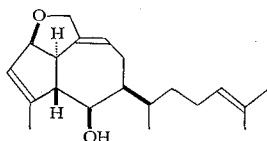
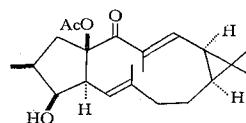
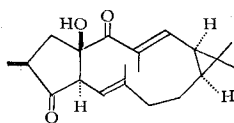
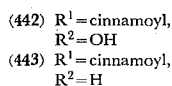
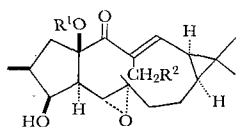
Chart 19

Jones oxidation of cembrene (433) has been carried out and the products were analyzed in detail.¹⁸³⁾ The conformation and relative stereochemistry of ovatodiolide (437) isolated from *Anisomeles ovata* were studied by ¹H NMR spectroscopy. X-ray analyses were also done to confirm the structures of ovatodiolide (437) and acid cyclization product 438.¹⁸⁴⁾ The molecular structure and absolute configuration of jatrophone (439),¹⁸⁵⁾ *p*-iodobenzoate (440) of jeunicin isolated from *Eunicea mammosa*,¹⁸⁶⁾ and new thunberganoid 441¹⁸⁷⁾ were determined by the X-ray analysis.

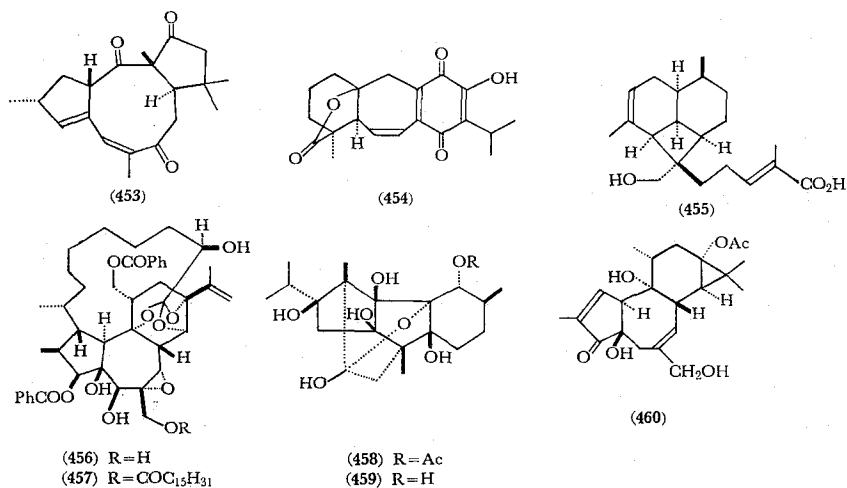


Four new diterpenes, jolkinols A (442), B (443), C (444), and D (445), were isolated from *Euphorbia jolkini*.¹⁸⁸⁾ The structures of dictyol A (446) and B (447) isolated from the brown alga, *Dictyota dichotoma*, were determined on the bases of spectroscopic and chemical evidence.¹⁸⁹⁾ These diterpenes were also isolated from the digestive gland of the molluscs, *Aplysia depilans*.¹⁹⁰⁾ Independent examination of the constituents of the red alga, *Sphaerococcus coronopifolius*, by two groups led to the isolation of closely related diterpenes, sphaerococcenol A (448)¹⁹¹⁾ and bromosphaerocoll (449).¹⁹²⁾

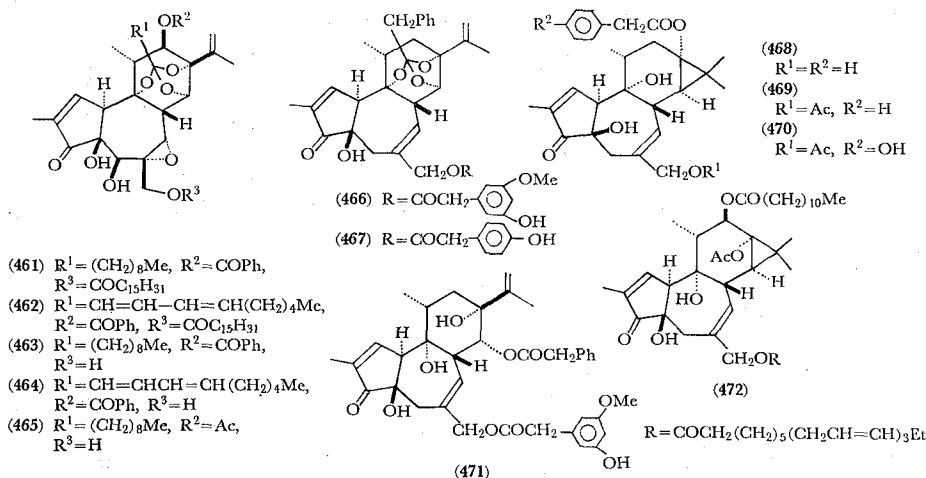
Uniquely different class of diterpenes were isolated from the marine animal



sources. One of them was isolated from *Dollabella californica* and assigned structure 450.¹⁹³ Dolatriol (451) and dolatriol 6-acetate (452) were isolated from *Dollabella auricularia*.¹⁹⁴ The structure of jatrophatrione (453), a constituent of the chloroform extract of *Jatropha macrorrhiza*, was determined by an X-ray analysis.¹⁹⁵ It was found to possess inhibitory activity toward the P-388 lymphocytic leukemia test system. The structure of icetexone (454) isolated from *Salvia ballotaeflorae* was determined from diffractometer data by direct methods.¹⁹⁶ Furthermore, X-ray analyses were effectively used for determination of several new diterpenes, 18-hydroxydecipia-2(4), 14-dien-1-oic acid (455) from *Eremophila decipiens*,¹⁹⁷ gnidimacrin (456) and its 20-palmitate (457), macrocyclic antileukemic diterpenoid esters from *Gnidia subcordata*¹⁹⁸, cinnzeylanine (458) and cinnzeylanol (459) from *Cinnamomum zeylanicum*,¹⁹⁹ and prostratin (460) from *Pimelea prostrata*.²⁰⁰



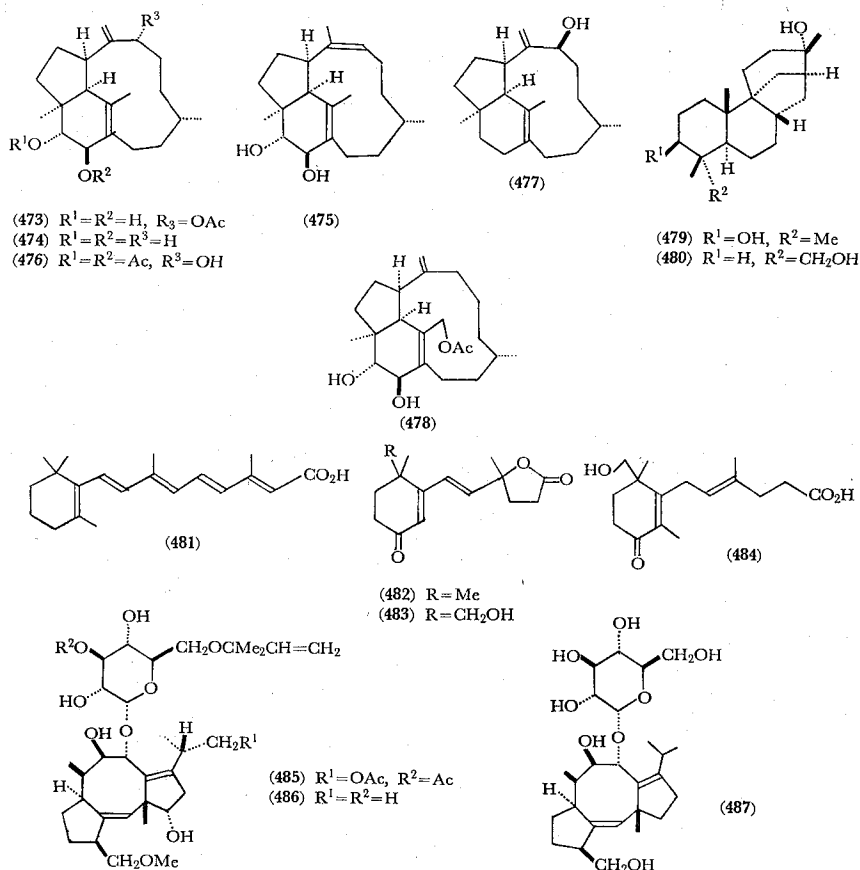
Chemical evidence for prostratin (460) was given by Hecker *et al.*²⁰¹ The new potent antileukemic principles, gnidilatin 20-palmitate (461), gnidilatidin 20-palmitate



(462), and gnidilatin (463), and the new toxic diterpenoids, gnidilatidin (464) and gnidiglaucin (465) were isolated from *Gnidia* species.²⁰²⁾ Gnidilatidin (464) was independently isolated from *Daphne odora* as a nematocidal constituent named odoracin.²⁰³⁾

From the resin isolated from latex of *Euphorbia poissonii* in Nigeria, four diterpenoids, 466-469, were isolated. Among these, 467 and 468 were new natural products.²⁰⁴⁾ The dried latex of the same plant was exhaustively extracted with acetone, from which compounds 470 and 471 were isolated.²⁰⁵⁾ A new cryptic irritant and cocarcinogen 472 was isolated from seeds of *Croton sparciflorus*.²⁰⁶⁾

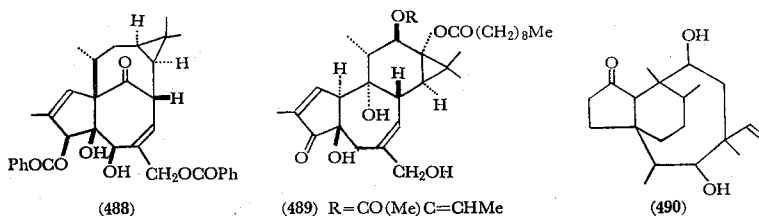
The structure of TG-2 (473), one of the major constituents of the soldier secretions of *Tinervitermes graciosus*, was determined by an X-ray analysis.²⁰⁷⁾ Five other congeners TG-1 (474), TG-3 (475), and TG-4 (476) from *T. graciosus*, TB-1 (477) and TB-3 (478) from *T. bettonianus*, were isolated and their structures were elucidated from spectral studies.²⁰⁸⁾ TG-1 was identical with TB-2 isolated from *T. bettonianus*.



Two new diterpenes, maritinol (479) and stemodinol (480), were isolated from *Stemodia maritima*.²⁰⁹⁾ After the intraperitoneal administration of retinoic acid (481) to rats, three urinary metabolites 482, 483, and 484 were isolated and identified.²¹⁰⁾

Biosynthetic studies of fusicoccin (485) and fusicoccin J (486) and H (487) using [3-¹³C]mevalonic acid lactone revealed that a polyprenyl pyrophosphate precursor cyclizes in a manner different to that previously observed in the biosynthesis of the ophiobolins.²¹¹⁾

Ingenol 3, 20-dibenzoate (488) and phorbol 12-tiglate 13-decanoate (489) were isolated from *Euphorbia esula* and *Croton tiglium*, respectively and characterized as antileukemic components.²¹²⁾ A number of derivatives of pleuromutilin (490) were prepared^{213,214)} and bactericidal activity of some derivatives were tested.²¹³⁾ The structural relationship of phorbol-12-myristate-13-acetate and cortisol was discussed and a possible mechanism for the tumor promoting activity of phorbol was presented.²¹⁵⁾

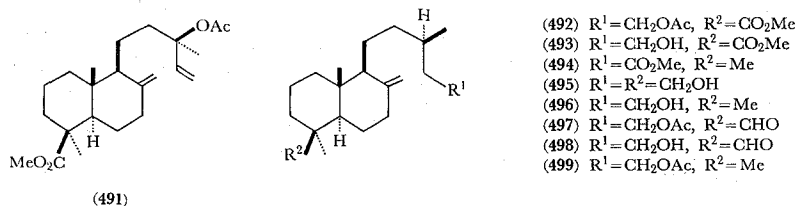


Many kinds of diterpene resin acids were isolated from *Pinus densiflora* needles and cortex.²¹⁶⁾ Isolation of free *cis*- and *trans*-phytol from the red alga *Gracilaria andersoniana* was reported.²¹⁷⁾

In a review titled "Diterpenoids of *Isodon* and *Teucrium* Plants", many kaurane- and clerodane-derivatives were described.²¹⁸⁾ In a review titled "Biosynthetic Studies with ¹³C-Labeled Precursors", examples on some diterpenoids, *e.g.* virescenol B, gibberellic acid, aphidicolin, and fusicoccin, were described.⁵⁶⁾ Another review concerning the biosynthesis of isoprenoids appeared in Japanese.²¹⁹⁾

ADDENDUM TO III.

The bleb resin of *Araucaria imbricata* (*A. araucana*) was examined and nine labdane derivatives, 491-499, were isolated.²²⁰⁾ Among them, compounds 492, 495, and 497 had been reported.



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