The Chemistry on Diterpenoids in 1966

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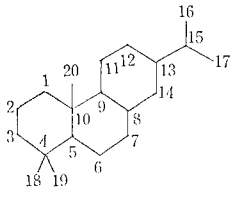
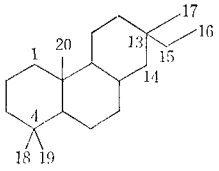
I. INTRODUCTION

The author has published the reviews on the chemistry on diterpenoids in 1964[1] and 1965.[2] The present review deals with an outline of the chemical works on diterpenoids in 1966.

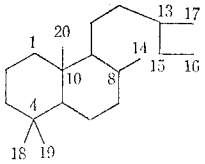
The classification consists of abietanes, pimaranes, labdanes, kauranes, gibbanes, diterpene alkaloids, and the others.



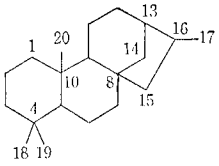
Abietane



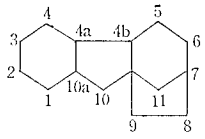
Pimarane



Labdane



Kaurane

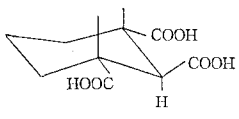


Gibbane

II. ABIETANE AND ITS RELATED SKELETONS

Thomas[3] investigated the constituents of the resins of *Agathis australis* and reported the isolation of abietic acid together with other diterpenes (see also sections III and IV).

Banerjee *et al.*[4] synthesized 1(*a*), 3(*a*)-dimethylcyclohexane-1-(*e*), 2(*e*), 3(*e*)-tricarboxylic acid (**1**) and 1(*a*), 3(*e*)-dimethylcyclohexane-1(*e*), 2(*e*), 3(*a*)-tricarboxylic acid (2), degradation products of diterpene acids.



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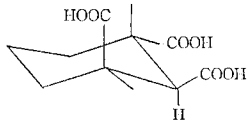

(2)

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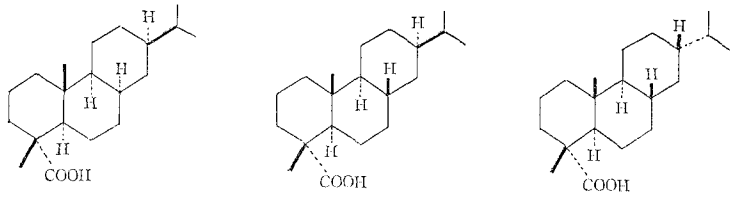
Parkin *et al.*[5] described the process of a large scale production of levopimaric acid-formaldehyde adduct from the pine gum or from the purified levopimaric acid. They prepared 6-hydroxymethylabietic acid from the adduct. The thermal reaction of abietic acid or rosin with formaldehyde was also investigated.

Herz *et al.*[6] prepared three kinds of abietanoic acids by an unambiguous method and they revised the previous assignments of the some acids as shown in Chart 1.



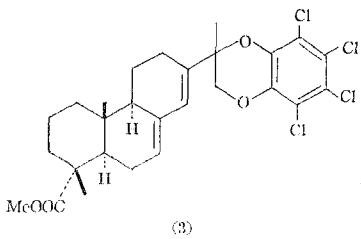
m.p. 168°
$[\alpha]_D$+23°

m.p. 202°
$[\alpha]_D$+17°

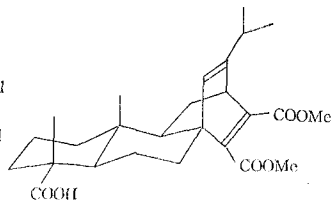
m.p. 179°
$[\alpha]_D$+10°

Chart 1

A total synthesis of (±)-dehydroabietic acid was described by Kierstad.[7] *2 The structure of a solid adduct which was obtained by the treatment of methyl abietate with tetrachloro-*o*-benzoquinone in xylene was shown by an Indian group[8] to be represented by formula 3.



(3)



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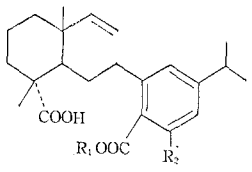
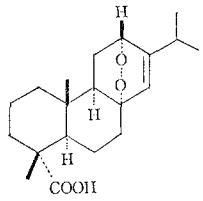


(5) : R_1=Me, R_2=COOMe
(6) : R_1=Et, R_2=H
(7) : R_1=Et, R_2=Ph

Herz *et al.*[9] studied the diene synthesis of levopimaric acid with acetylene dienophiles. A thermal rearrangement of the adduct 4 yielded a product 5. Levopimaric acid and ethyl propiolate were refluxed in a nitrogen atmosphere for four hours to give a product 6. Similarly, the reaction of levopimaric acid with ethyl phenylpropiolate at 210—220° for four hours in a nitrogen atmosphere yielded product 7.

Levopimaric acid transannular peroxide (8) was treated with ferrous sulfate to give dioxide 9.[10] A reaction of levopimaric acid with *m*-chloroperbenzoic acid in aq. ethanol gave 12α-hydroxyabietic acid (10) and 8α, 12α-dihydroxy Δ^{13}-dihydroabietic acid (11). The reaction mechanism was discussed by Lawrence *et al.*,[10]

*2 See later (ref. 19).



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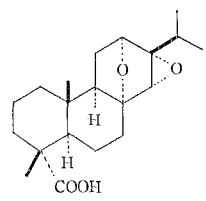

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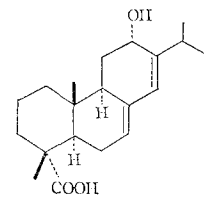

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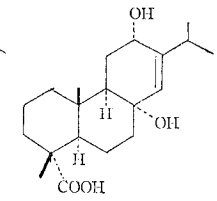
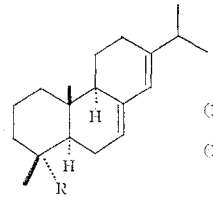


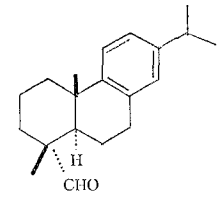
(11)

Westfelt[11] studied the extracts from fresh and fungus infested wood of *Pinus silvestris*. Abietinol (12), abietinal (13), and dehydroabietinal (14) were found in both extracts. (See also section III.)



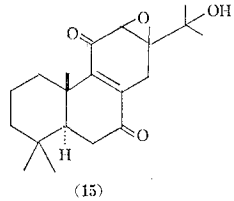
(12) : R=CH_2OH

(13) : R=CHO



(14)

The leaf of *Callicarpa candicans* has long been used for stupefying fishes by the natives of Palau and Philippine Islands. Kawazu and Mitsui[12] isolated an acitve principle which was named callicarpone, and proposed structure **15** to it. The stereochemistry of the epoxide ring remains unsolved.



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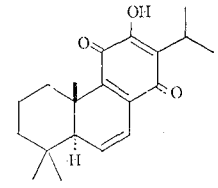
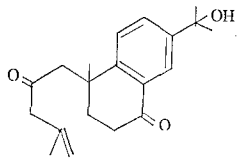


(16)

(17) : 6, 7-saturated

Gough and Sutherland[13] carried out a steam-distillation of the leaves and stems of a suspected mixture of *Plectranthus* species, and got a little essential oil and some orange crystals in a 0.025% yield. The latter proved to be identical with dehydroroyleanone (16).[14] Royleanone (17)[14] was also shown to be present as a relative minor constituent.

Anthonsen[15] refuted the suggestion[16] that the diterpenoid, $C_{20}H_{28}O_3$, m.p. 131-132° (Solidago-diterpene A[2]), isolated from certain *Solidago* species, has the struc-



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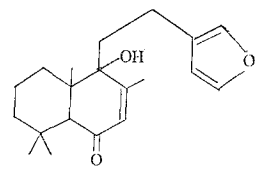

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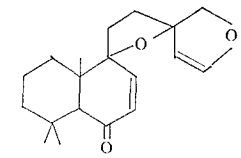


(20)

ture 18. Subsequently, he and his collaborators[17] suggested the structural formula 19 to this compound, which they gave the name "solidagenone". Solidagenone may well be an artifact, because they did not get solidagenone on treatment of a light-petroleum extract, but they got a mixture of epimers at C-13 of compound 20, which on refluxing with ethanol gave solidagenone in a high yield. The stereochemistry of solidagenone remains unsolved.

Mori and Matsui[18] synthesized methyl (±)-13-oxopodocarp-8(14)-en-16-oate (as 22), an important intermediate for the diterpenoid synthesis, *via* (±)-deoxypodocarpic acid (as 21). The outline is shown in Chart 2.

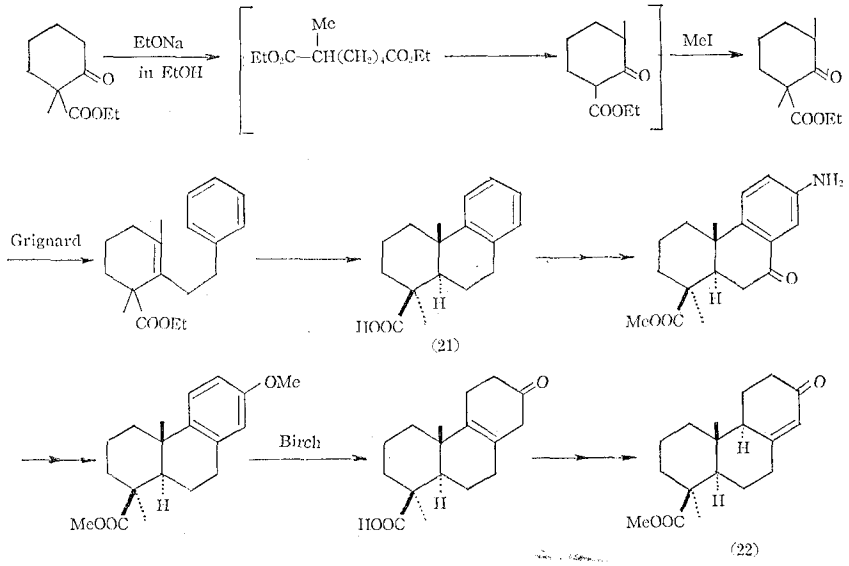
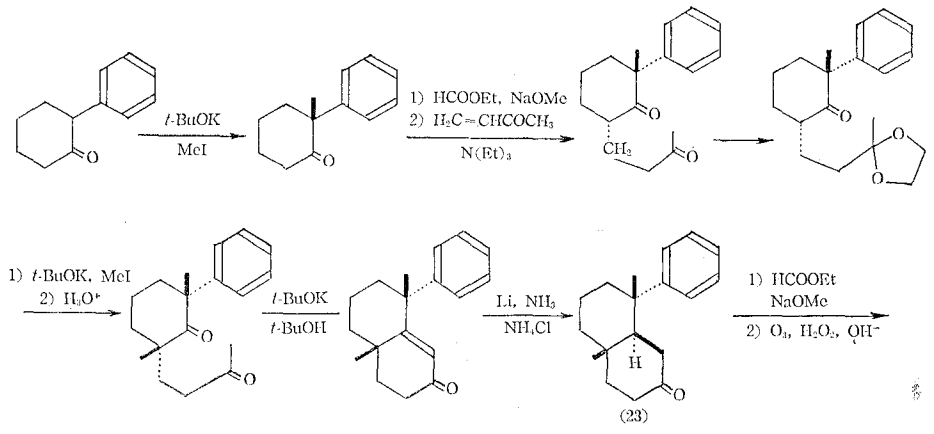


Chart 2

Ireland and Kierstead[19] synthesized (±)-deisopropyldehydroabietic acid (as 24) *via* 4β, 9β-dimethyl-4α-phenyl-*trans*-decalone-6 (as 23) in 10% overall yield. (See chart 3.)



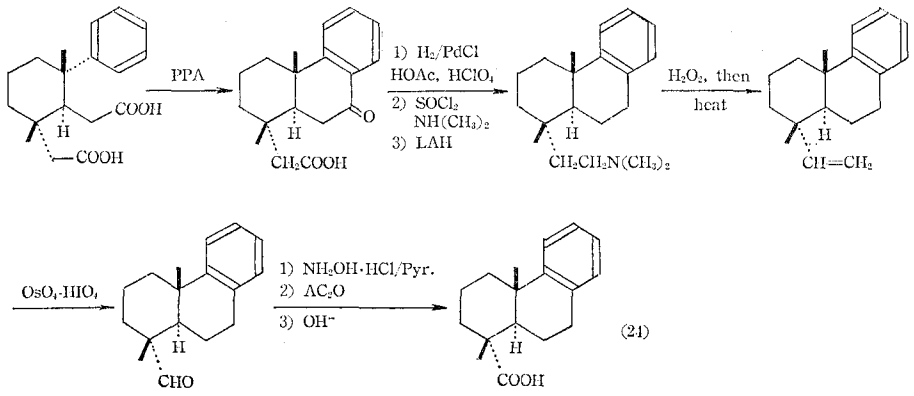
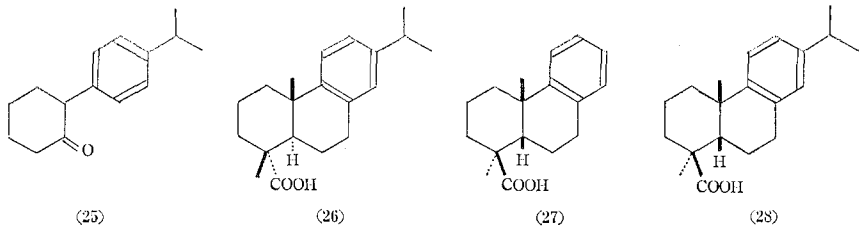


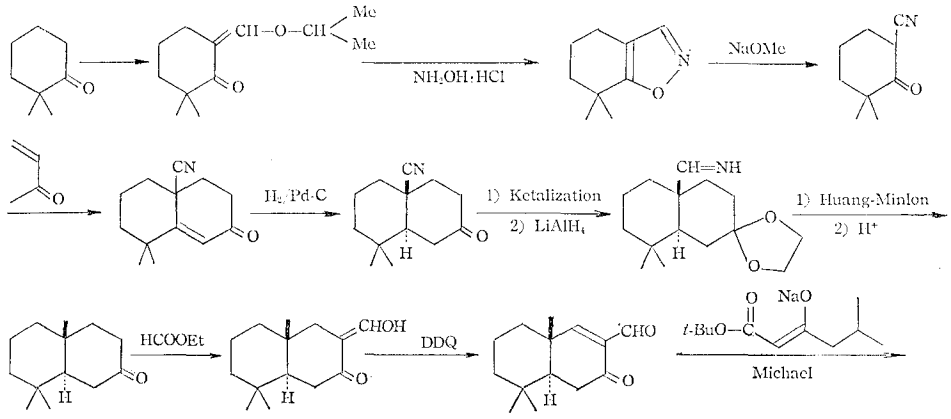
Chart 3

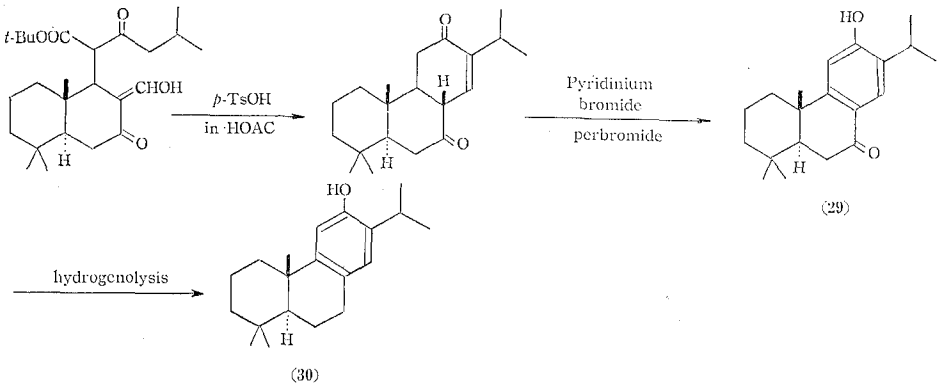
They applied this procedure to 2-*p*-isopropylphenylcyclohexanone (25) and synthesized (±)-dehydroabietic acid (as 26) in 18% overall yield.



A modification of this scheme made it possible to synthesize (±)-4, 5-isodeisopropyldehydroabietic acid (as 27) and (±)-4, 5-isodehydroabietic acid (as 28).

The total sytheses of (±)-sugiol (as 29) and (±)-ferruginol (as 30) were accomplished by Meyer *et al.*.[20] The route is shown in Chart 4.

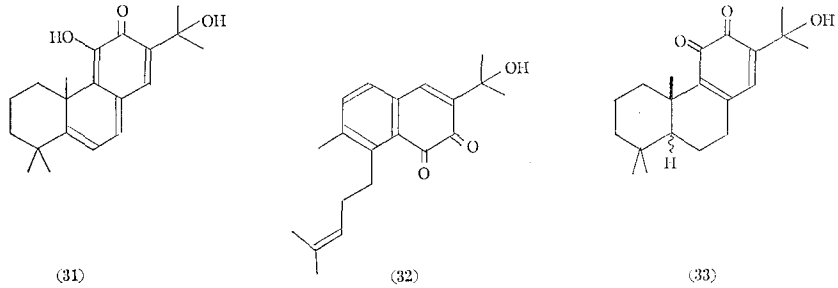




(29) (30)

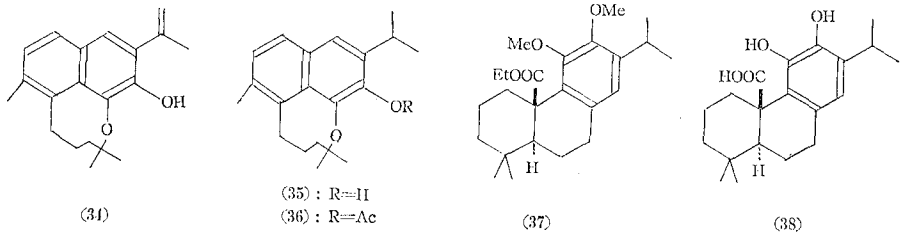
Chart 4

Eugster *et al.*[21] isolated fuerstion, a red pigment, from the leaves of *Fuerstia africana* and suggested structure **31** to this material. Fuerstion is very sensitive to nucleophilic as well as electrophilic reagents. Treatment with acid caused an opening of the ring A accompanied by a rearrangement and gave 1, 2-naphthohydroquinone which was subjected to oxidation to orthonaphthoquinone (fuerstionone) (**32**). Catalytic reduction of fuerstion followed by oxidation with silber oxide gave an orthoquinone **33**. Clemmensen reaction with fuerstion afforded the rearranged naphthalene derivatives **34** and **35**. The N.M.R. spectra of **35** and **36** indicated that the methyl groups of their aromatic isopropyl group are magnetically non-equivalent. The details of the N.M.R. spectrum of **35** were investigated by variable temperature, and the above effect was shown to be due to a consequence of conformational chirality.[22]



(31) (32) (33)

Meyer and Schindler[23] synthesized ethyl (±)-carnosate dimethyl ether (as **37**). Since the (+)-enantiomer has been converted to carnosic acid (**38**), only the resolution step of the racemic compound **37** remains for the accomplishment of the total synthesis of carnosic acid.



(34) (35) : R=H (36) : R=Ac (37) (38)

Enzell[24] applied the method of refluxing the compounds with amalgamated zinc and a mixture of deuteriochloric and deuterioacetic acids to several podocarpa-8, 11, 13-triene derivatives and introduced deuterium to the desired positions. Some pertinent examples are shown in Chart 5.

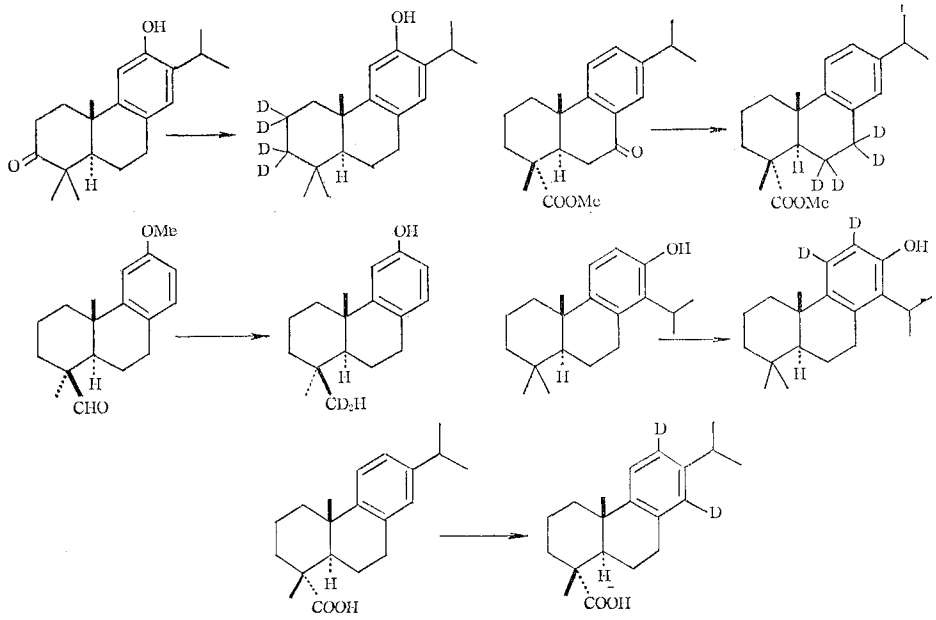
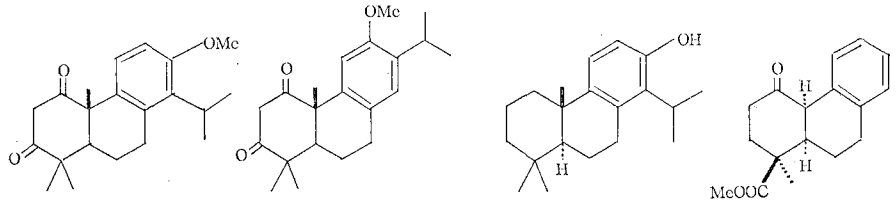


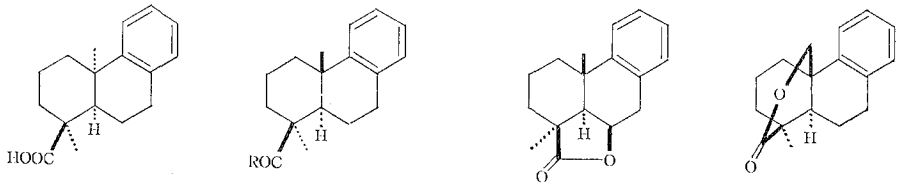
Chart 5

Mangoni and Belardini[25] isolated two terpene ketones **39** and **40** from the *Cupressus sempervirens* gum.



(39) (40) (41) (42)

Bennett and Cambie[26] studied the method of reduction of the aromatic ring of totarol (**41**). Enzell[27] studied the mass spectra of totarol (**41**) and other several aromatic diterpenes, and analyzed the fragmentation. Dasgupta and



(43) (44) : R=OH (45) : R=NH_2 (46) (47)

Antony[28] synthesized compound 42 (racemate), which was converted to (±)-deisopropyl-*cis*-dehydroabietic acid (as 43) and (±)-deoxypodocarpic acid (as 44).

Mori and Matsui[29] carried out the photochemical lactonization on (±)-deoxypodocarpamide (as 45) and got two lactones, the racemates of 46 and 47. The yield of the product 46 was 8–12%, while that of 47 was 2–3%.

Johnson *et al.*[30] found an efficient and sterospecific polyolefinic cyclization, and accomplished a total synthesis of (±)-fichtelite (as 48) using such a method as shown in Chart 6.

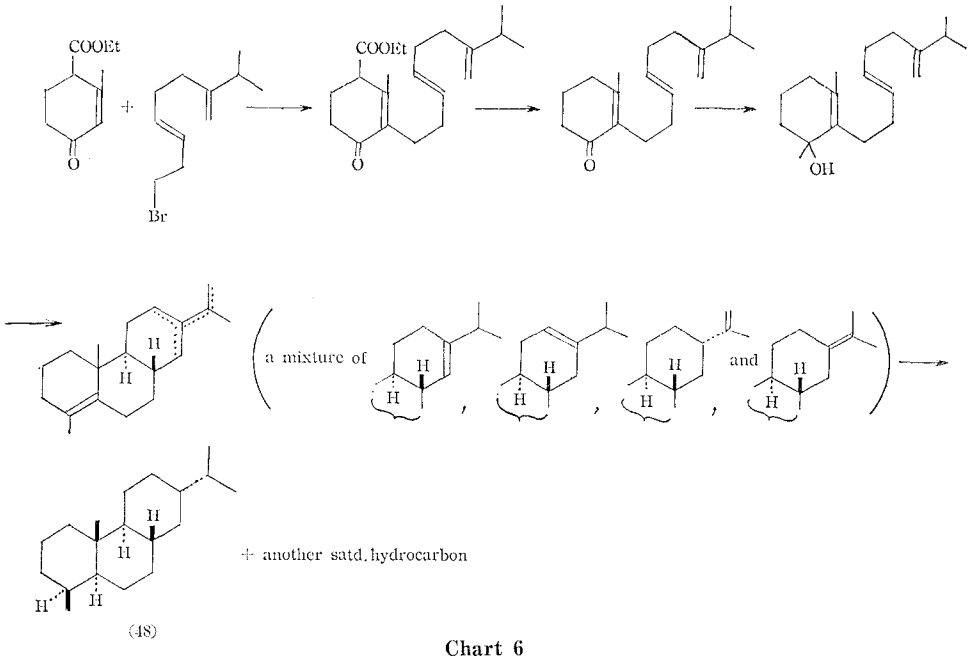


Chart 6

Chang and Pelletier[31] prepared a diterpene epoxy ε-lactone **51** from compound **49** and proved the sequence of **49**→**50**→**51**. (Chart 7) They also studied the rearrangements of compound **51** to **52** and deduced a mechanism.

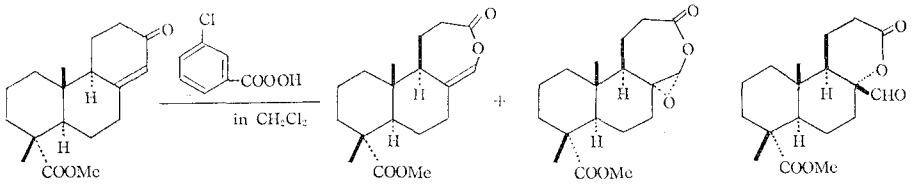
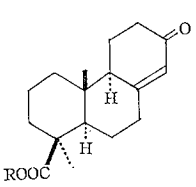
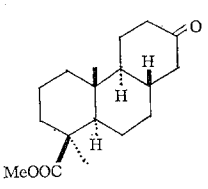


Chart 7

Barltrop and Day[32] carried out the resolution of (±)-**53** through its cinchonine salt and got (+)-keto ester (**54**) after methylation. Methyl (+)-13-oxopodocarp-8(14)-en-16-oate (**54**) was subjected to the catalytic reductions to give B/C *trans* dihydro derivative **55** as a sole or a major product. Keto ester **55** was allowed to react with perbenzoic acid to yield two isomeric ε-lactones **56** and **57**.



(53) : R=H
(54) : R=Me



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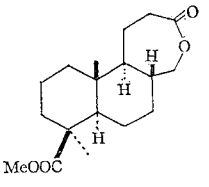

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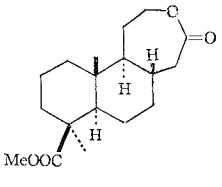
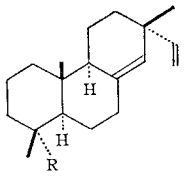


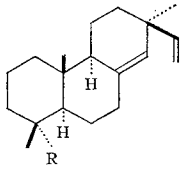
(57)

III. PIMARANE AND ITS RELATED SKELETONS

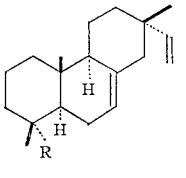
Thomas[3] isolated sandaracopimaric acid (**58**) and sandaracopimaradienol (**59**) from the resins of *Agathis australis*. Westfelt[11] isolated pimaradiene (**60**), pimari-



(58) : R=COOH
(59) : R=CH_2OH



(60) : R=Me
(61) : R=CH_2OH
(62) : R=CHO



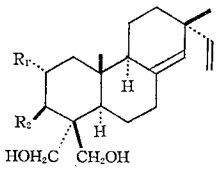
(63) : R=Me
(64) : R=CH_2OH
(65) : R=CHO

nol (**61**), pimarinal (**62**), isopimaradiene (**63**), isopimarinol (**64**), and isopimarinal (**65**) from the wood of *Pinus silvestris*. The same author[33] showed the presence of all the above pimarane derivatives in the Swedish sulfate turpentine (mainly derived from *Pinus silvestris*). Lawerence *et al.*[34] reported the presence of sandaracopimaric acid (**58**) and $\Delta^{8(9)}$-isopimaric acid as the consituents of pine oleoresin.

Whally *et al.*[35] investigated the anisotropies of the C—C, C—H, and C=C bonds, and applied their conceptions to sandaracopimaric, isopimaric, and pimaric acids, and their corresponding dihydro- and tetrahydro derivatives.[36] They calculated the chemical shift of the methyl proton signals at C-17, C-18, and C-20, and assigned the methyl resonances in the foregoing compounds.

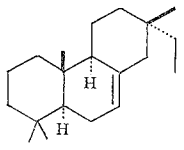
Fetizon and Golfier[37~39] converted 3β-hydroxyandrost-5-en-17-one into 4, 4-dimethyl-5α-androst-14-ene, whose stereochemistry was investigated. The latter compound was transformed into sandaracopimaradiene, which was shown to be identical with the authentic natural product sample.

Carman *et al.*[40] assigned the structures **66**, **67**, and **68** to the sublimed hexane insoluble materials, dacrydol D_1, D_2, and D_3, isolated from the extract of the heartwood of *Dacrydium colensoi*, respectively.

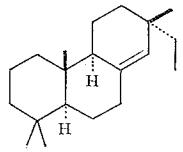


(66) : $R_1=R_2=OH$
(67) : $R_1=OH$, $R_2=H$
(68) : $R_1=H$, $R_2=OH$

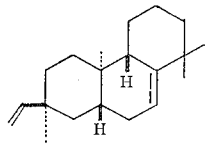
Enzell and Wallis[41] studied the optical rotatory dispersion of some pimarene derivatives. The Δ^7-compounds, the representative of which is isopimar-7-ene



(69)



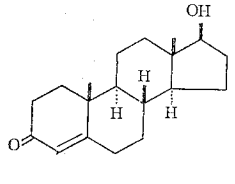
(70)



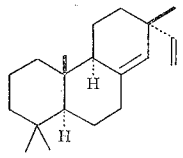
(71)

(69), show the negative plain curves, like cholest-5-ene. The simpler derivatives of $\Delta^{8(14)}$-compounds including isopimar-8(14)-ene (70) exhibit the positive plain curve like cholest-4-ene. In the case of 8(14), 15-dienes, the sign of the curve depends upon the steric configuration of a quaternary carbon atom at C-13 between two double bonds. Thus, sandaracopimaradiene (73) exhibits a negative curve, while pimaradiene (60) shows a very strong positive curve. The cyclic double bond of rimuene (71) has an environment enantiomeric to that of pimar-7-ene, hence rimuene exhibits a positive curve.

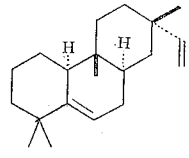
Johnston *et al.*[42] accomplished a chemical conversion of testosterone (72) into (−)-sandaracopimaradiene (73).



(72)



(73)

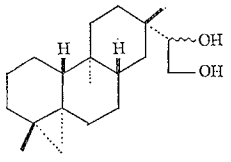


(74)

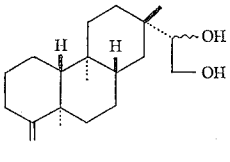
Connolly, Overtone *et al.*[43] *3 published a full paper on the constitution and stereochemistry of rimuene, establishing the correct formula 74. Soon after, Corbett and Wyllie[44] *3 also published a full paper on the structure of rimuene.

McCrindle, Overton *et al.*[45] published a full paper on the structures of erythroxydiols X, Y, and Z isolated from trunk wood of *Erythroxylon monoginum*. They gave the constitution and stereochemistry 75, 76 and 77 to erythroxydiols X, Y, and Z, respectively, as shown already in their communication.*3

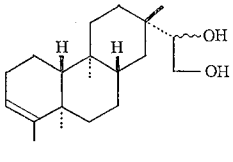
The further investigation by McCrindle *et al.* was carried out on erythroxytriols P and Q. They[46] presented the evidence for assignments of structure 78 to erythroxytriol P and of structure 79 to erythroxytriol Q. The subsequent X-ray analysis[47] of *p*-iodobenzoate (80) of triol Q acetonide established the full stereo-



(75)



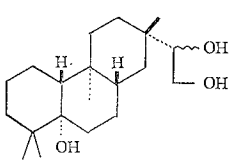
(76)



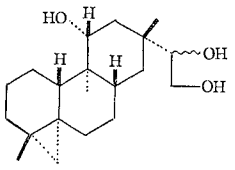
(77)

*3 See ref. 1.

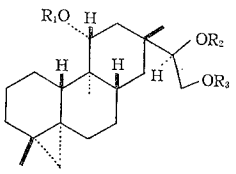
chemistry of erythroxytriol Q as shown in formula 81. Thus, a tentatively proposed structural formula 82 by Dev *et al.*[48] was shown to be not correct.



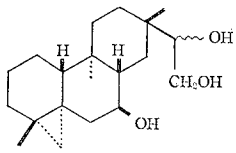
(78)



(79)

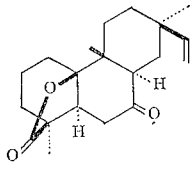


(80) : R_1=*p*-IC_6H_4CO, R_2, R_3=$Me_2C<$
(81) : R_1=R_2=R_3=H

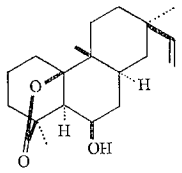


(82)

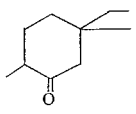
The absolute stereochemistry of rosenono-(83) and rosololactone (84) and of various derivatives was defined by application of the technique of optical rotatory dispersion.[49] *4



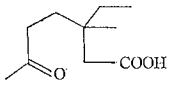
(83)



(84)



(85)



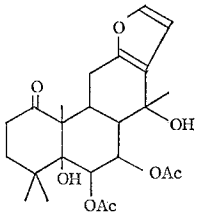
(86)

Whalley *et al.*[50] synthesized (±)-5-ethyl-2, 5-dimethylcyclohexanone (85) and (±)-3-ethyl-3-methyl-6-oxoheptanoic acid (86), the racemates of the corresponding optically active compounds derived from ring C of rosenonolactone (83).

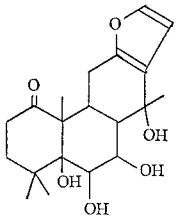
Scott *et al.*[51] reported hydroxyl, carbonyl, and carbon-carbon double bonds infrared absorption bands of rosenonolactone (83) and related diterpenoid lactones. They found that rosololactone (84) shows a marked tendency to dimerise through hydrogen bond formation, even at low concentrations in carbon tetrachloride.

The optical rotatory dispersion of rosenonolactone (83) and related compounds was studied by Klyne, Whalley *et al.*[52], and the lactone sector rule[53] was successfully applied to various lactones and related conpounds derived from the rosane skeleton.

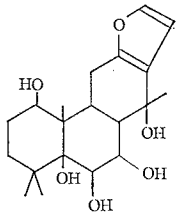
Canonica *et al.*[54] isolated α-caesalpin, β-caesalpin, and γ-caesalpin from the seeds of *Caesalpinia bonducella*. γ-Caesalpin was refluxed in *N*-potassium hydroxide in ethanol for 4 hours to yield δ-caesalpin. They presented the partial structure



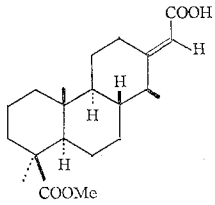
(87)



(88)



(89)

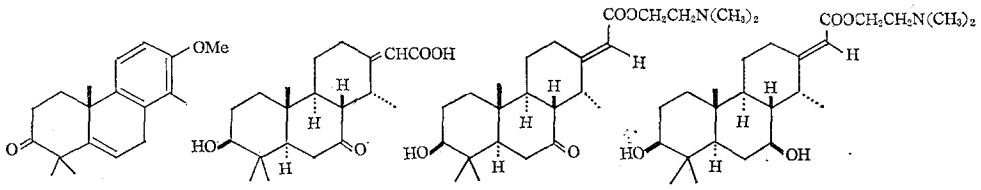


(90)

*4 See refs. 1 and 2.

to caesalpins[55], and subsequently, proposed structures 87, 88, and 89 for α-, β-, and δ-caesalpin, respectively.[56]

Mori and Matsui[57] published the total synthesis of C-14 epimer (as **90**) of (±)-7-deoxocassamic acid and its derivatives. They also gave some discussion on the stereochemistry at C-14. Traverso *et al.*[58] synthesized (±)-deoxocassaic acid from compound **91**.

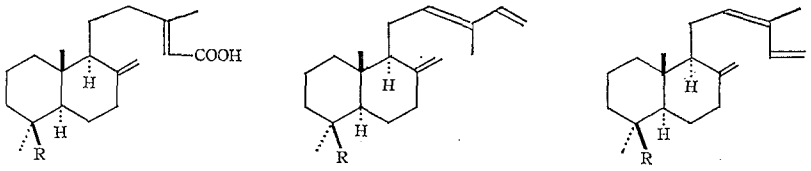


(91) (92) (93) (94)

Turner *et al.*[59] established the structure **92** of cassaic acid, and accomplished its total synthesis. The synthesis means the total synthesis of cassaine (**93**) and of cassaidine (**94**), *Erythrophleum* alkaloids.

IV. LABDANE AND ITS RELATED SKELETONS

Agathic acid (**95**), its mono methyl ester (**96**), *trans*-communic acid (**97**), *trans*-communol (**98**), *cis*-communic acid (**99**), and *cis*-communol (**100**) were isolated from the resins of *Agathis australis*.[3]

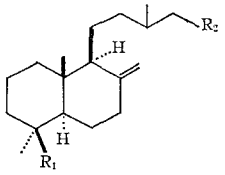


(95) : R=COOH
(96) : R=COOMe

(97) : R=COOH
(98) : R=CH_2OH

(99) : R=COOH
(100) : R=CH_2OH

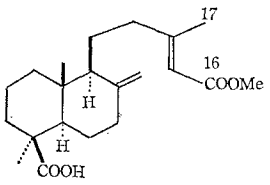
Bruns and Weissman[60] isolated a series of labdane derivatives from the resins of *Araucaria imbricata*, and described their steric configuration. They are listed up in Chart 8. The plane structures were already reported.[61]



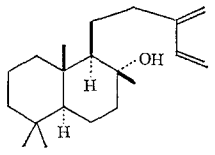
R_1=COOH, R_2=CH_2OH: Imbricatolic acid
R_1=COOH, R_2=CH_2OAc: Imbricatolic acid acetate
R_1=R_2=CH_2OH: Imbricatadiol
R_1=CHO, R_2=CH_2OH: Imbricatolal
R_1=CHO, R_2=CH_2OAc: Imbricatolal acetate

Chart 8

Carman and Marty[62] isolated a new methyl ester of agathic acid from *Agathis microstachya* oleoresin and proved it to be C-16 methyl ester (**101**).



(101)



(102)

Chirkova *et al.*[63] isolated isoabienol (**102**) besides other diterpenes from the oleoresin of *Abies sibirica*.

Ourisson *et al.*[64] isolated seven kinds of new bicarbocyclic diterpenes from *Trachylobium verrucosum*. Their structure and stereochemistry are shown in Chart 9.

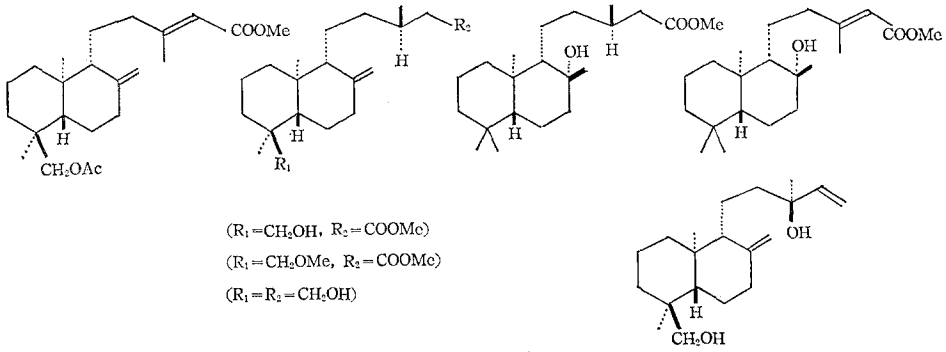
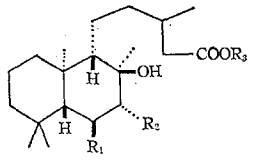


Chart 9

Jefferies *et al.*[65] isolated three new diterpenes, that is, 8β-hydroxy-*enantio*-labdan-16-oic acid (**103**), 6β, 8β-dihydroxy-*enantio*-labdan-16-oic acid (**104**), and 7α, 8β-dihydroxy-*enantio*-labdan-16-oic acid (**105**) from *Dodonaea lobulata*.

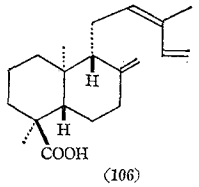


(103) : $R_1=R_2=R_3=H$

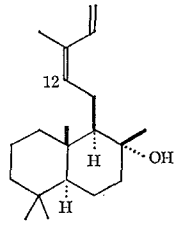
(104) : $R_1=OH$, $R_2=R_3=H$

(105) : $R_1=R_3=H$, $R_2=OH$

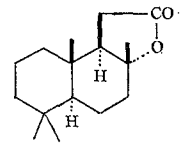
Bevan *et al.*[66] reported the isolation of a new diterpenic acid, which was called ozic acid (**106**), from *Daniellia ogea*.



(106)



(107)



(108)

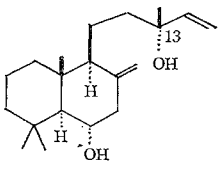
Carman[67] gave a discussion on the correlation between the optical rotation and the structure on the basis of the molecular rotations of 143 kinds of labdane

derivatives, but no simple relation between them was found.

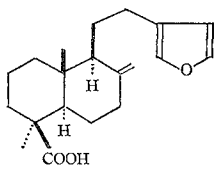
Carman[68] elucidated the absolute configuration of abienol (**107**) through its chemical conversion into the known (+)-norambreinolide (**108**).[69] The evidence for the *cis* nature of Δ^{12} double bond in **107** was provided by the N.M.R. spectrum.

Sandermann and Bruns[70] revised their previous assignment for the stereochemistry at C-13 of larixol to that shown in formula **109**, which was in good agreement with the assignment of Norin *et al.*.[71]

A new diterpenic acid, lambertianic acid, was isolated from the oleoresin of *Pinus lambertiana* by Dauben and German.[72] The structure proved to be represented as **110**, which corresponded to the optical antipode of daniellic acid.



(109)

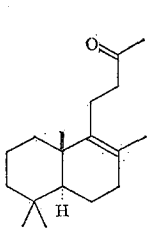


(110)

Boyle[73] succeeded in separation of two diastereoisomers, epimeric at the β-position of the tetrahydrofuran ring, after hydrogenation of marrubiin in glacial acetic acid over 10% palladised barium sulfate.

Vlad *et al.*[74] refluxed sclareol with acetic anhydride, and chromatographed the product on an alumina column. They got 13-*epi*manoyl oxide and manoyl oxide.

Wenkert *et al.*[75] converted methyl neoabietate into an unsaturated ketone (**111**), which had been transformed into sclareol (**112**), manool (**113**), and manoyl oxide



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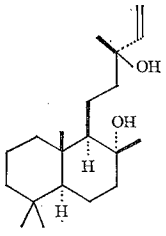

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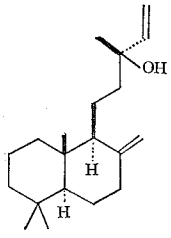
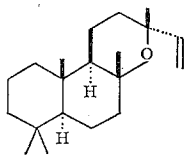
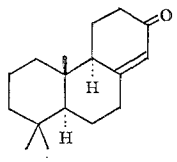


(113)



(114)



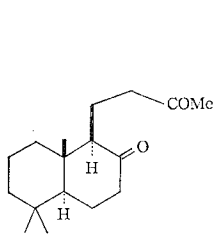
(115)

(**114**). This means the total syntheses of the latter compounds. In this course, compound **115** was necessary in a large quantity as an intermediate, so the oxidation of *t*-butanolic solution of manool (**113**) with periodic acid in the presence of a trace quantity of osmium was carried out in order to prepare its material **116**.

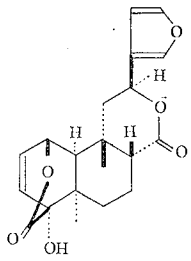
Vlad *et al.*[76] synthesized 13-*epi*manool from 13-*epi*sclareol.

Overton *et al.*[77] studied the stereochemistry of the *Colombo* root bitter principles. They deduced the stereochemistry and absolute configuration of **117** for columbin and of **118** for isocolumbin on the basis of chemical, spectroscopic, and optical rotatory dispersion studies.

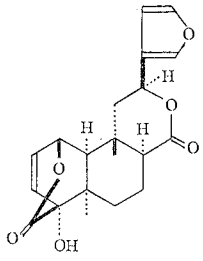
Robertson, Sim, *et al.*[78] carried out X-ray analysis of the 1-*p*-iodophenyl-3-phenylpyrazoline adduct of isocolumbin and established the absolute configuration



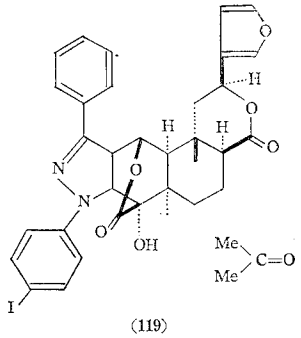
(116)



(117)

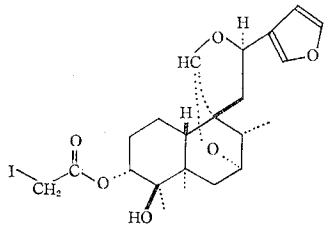


(118)

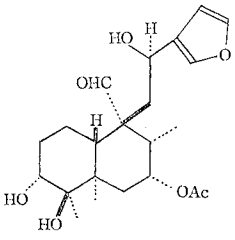


(119)

119 for it, hence the structure and absolute configuration of isocolumbin were established as **118**.



(120)



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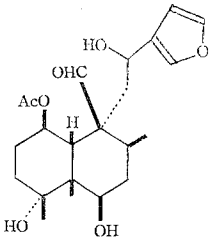
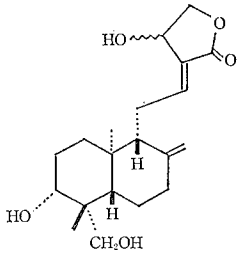
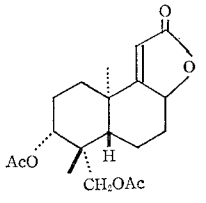


(122)

Sim *et al.*[79] carried out the X-ray analysis of deacetylcascarillin acetal iodoacetate and established its structure and absolute configuration as **120**. Hence, the structure and absolute configuration of cascarillin itself, a bitter principle of *Cascarilla bark* (*Croton eleuteria*), was established as **121**. Thus, the previous assignment of **122** (or its mirror image) to the same substance by Halsall[80] was revised.



(123)



(124)

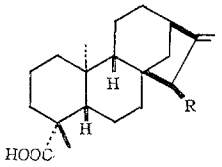
Pelletier *et al.*[81] carried out a stereospecific synthesis of the compound **124** which had been derived from andrographolide (**123**) by acetylation, ozonolysis and treatment with acetyl chloride. This reconfirmed the structure and stereochemistry of the rings A and B of andrographolide.

V. KAURANE AND ITS RELATED SKELETONS

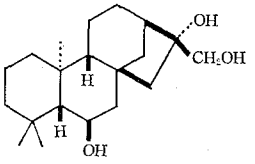
Two diterpenic acid, (−)-kaur-16-en-19-oic acid (**125**) and 15β-hydroxy-(−)-

kaur-16-en-19-oic acid (**126**), were isolated from *Phebalium rude* by Jefferies *et al.*.[82] This provides the first example of the isolation of diterpenes from Rutaceous plant.

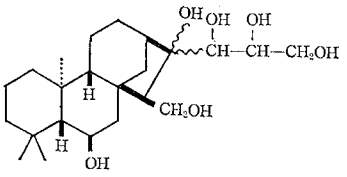
Pérezamador and Jiménez[83] isolated a new diterpenic alcohol, corymbol, as well as its diacetate and triacetate, from *Turbina corymbosa*. The structure and absolute configuration of corymbol were determined as shown in formula **127**. A biogenesis of turbicorytin (**128**) from corymbol was discussed.



(125) : R=H
(126) : R=OH

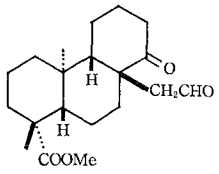


(127)

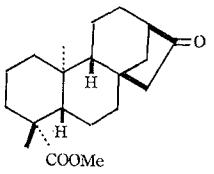


(128)

Mori and Matsui[84] accomplished the total synthesis of (±)-kaur-16-en-19-oic acid (as **125**) ; they synthesized a key intermediate **129** (represented as an enantiomer) through thirteen steps and converted it to (±)-keto ester (as **130**) by cyclization of the D-ring with sodium methoxide, protection as tetrahydropyranyl ether, Wolff-Kishner reduction, acidic hydrolysis to alcoholic acid, Jones' oxidation, and esterification.

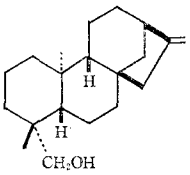


(129)

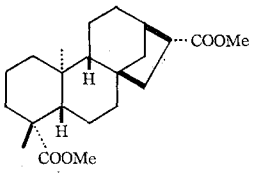


(130)

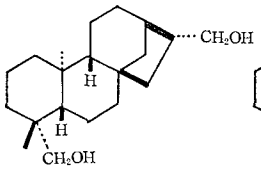
Since the conversion of keto ester **130** into kaur-16-en-19-oic acid has been accomplished, the synthesis means a total synthesis of (±)-kaur-16-en-19-oic acid.



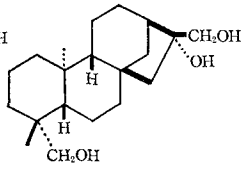
(131)



(132)



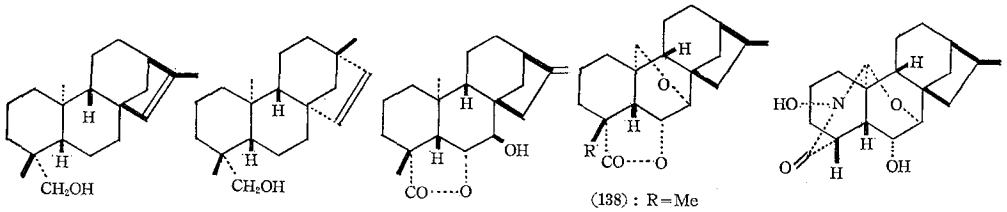
(133)



(134)

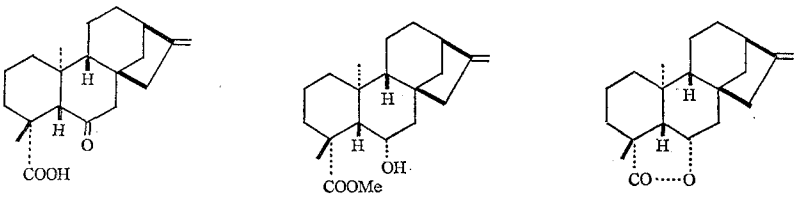
Subsequently, Sumiki, Matsui *et al.*[85] carried out a total synthesis of (±) kaur-16-en-19-ol (as **131**) *via* (±)-keto ester **130**. They converted (±)-**131** to (±)-17, 19-diester **132** *via* five steps, which means also the total syntheses of the racemates of natural diterpene diol **133**[86] and triol **134**[86] isolated from Australian shrub. Moreover, the acetate of the racemic compound **131** was refluxed with xylene containing a small quantity of iodine for nine hours. An alkaline hydrolysis and chromatography on silica gel column containing silver nitrate resulted in the sparation into unreacted material, (±)-isokaurenol (as **135**), and (±)-monogynol (as

136). Hence, their total syntheses were also accomplished.



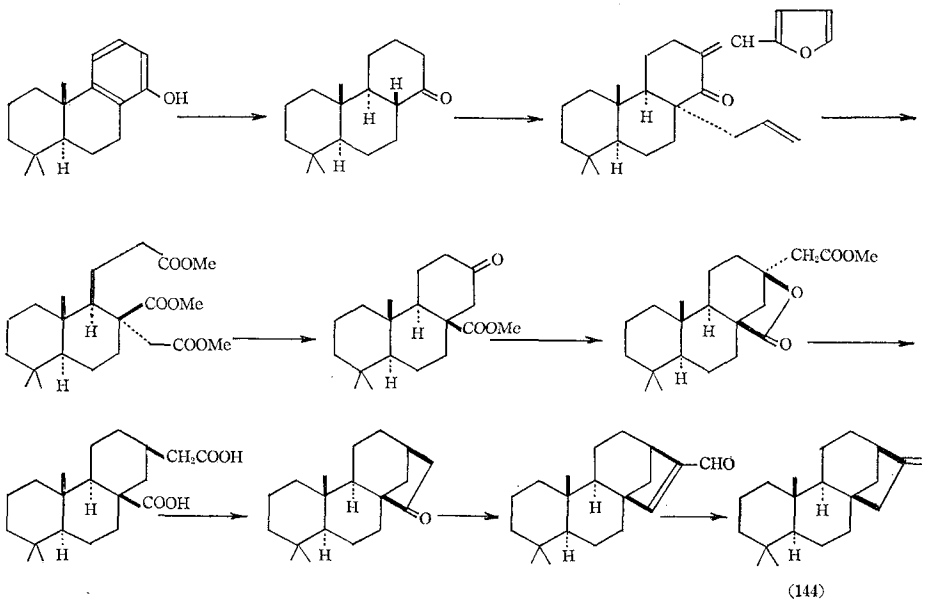
(135) (136) (137) (138) : R=Me (139) : R=H (140)

Hanson[87] investigated the oxidation of Δ^{16}-terminal methylene group in 7-hydroxykaurenolide (**137**) with various reagents. He[88] studied the N.M.R. spectra on kaurenolides and found that the B-ring of kaurenolides is present as a twisted boat form. He also prepared some 7α-20 ethers—*e.g.* **138**, **139**, and **140**—by photolytic methods. The same author[89] converted 7β-hydroxykaurenolide (**137**) into 6α-hydroxy-(−)-kaur-16-en-19-oic acid 19→6α lactone (**143**) *via* **141** and **142**. 7α-Hydroxykaurenolide was similarly converted to **143**.



(141) (142) (143)

Galt and Hanson[90] published a detailed full paper of a preliminary communication reported already in 1964[41]; they converted 7β-hydroxykaurenolide (**137**) into (−)-kaur-16-en-19-oic acid (**125**).

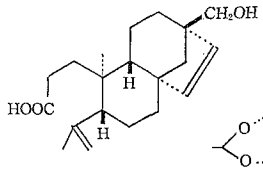


(144)

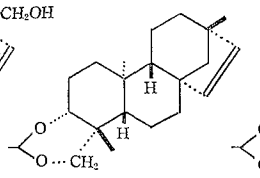
Chart 10

Yoshikoshi *et al.*[91] reported their N.M.R. studies of many kaurane derivatives.

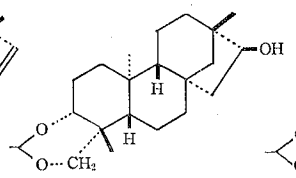
Turner *et al.*[92] published a full paper of a stereospecific, total synthesis of phyllocladene (144). The outline of the synthesis is shown in Chart 10.



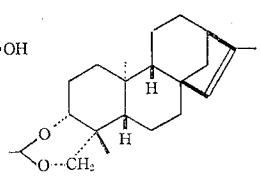
(145)



(146)



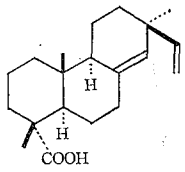
(147)



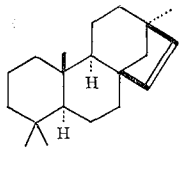
(148)

Ghisalberti and Jefferies[93] isolated a secobeyerene 145 from the ethereal extract of *Beyeria sp. nov.* The same authors[94] tried a rearrangement of the beyerene skeleton to (−)-kaurene skeleton. They prepared an epoxide from 3α, 19-ethylidenedioxybeyer-15-ene (146) and treated it with lithium in ethylamine to give a suitable 16-exo alcohol 147. The alcohol was converted to the tosylate, which was treated with sodium acetate in acetic acid to yield a mixture of 146 and 148.

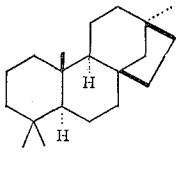
Herz *et al.*[95] carried out the partial synthesis of (−)-hibaene (150) and (−)-hibane (151) from pimaric acid (149). The common intermediate was 152.



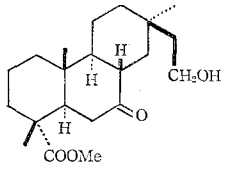
(149)



(150)

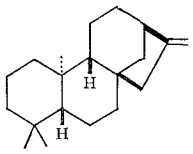


(151)

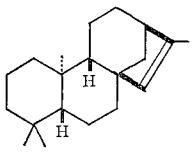


(152)

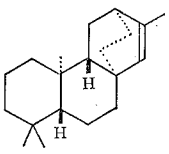
Sobti and Dev[96] converted a 16-alcohol which was obtained by hydroboration of (+)-hibaene (antipode of 150) into tosylate and carried out the solvolysis of the latter in buffered, 66% aq. dioxane, and they got a hydrocarbon mixture (40%) and an alcohol (60%). The chromatography of the former mixture on a silica gel column containing silver nitrate separated (−)-kaurene (153), (−)-isokaurene (154) and (+)-hibaene.



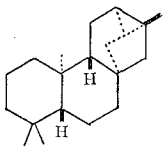
(153)



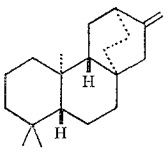
(154)



(155)



(156)



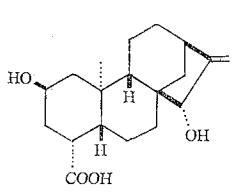
(157)

Murray *et al.*[97] tried also the rearrangement of (+)-stachene ((+)-hibaene) into (−)-kaurene (153) and (−)-isokaurene (154). They investigated the action of dry hydrogen chloride in various solvents on (+)-stachene itself.

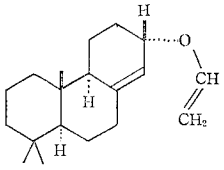
Subsequently, Murray *et al.*[98] used a combination of thin layer chromatography, gas liquid chromatography, and combined gas chromatography and mass spectrometry to study the isomerisation, under conditions analogous to those used for stachene, of other members of the same series, namely (−)-kaurene (153), (−)-isoatisirene (155), and (−)-trachylobane (156). The results were as follows;

stachene, trachylobane, and kaurene were converted into mixtures of atisirene (**157**), isoatisirene (**155**), kaurene (**153**), and isokaurene (**154**). Isoatisirene furnished an equilibrium mixture of starting material and atisirene.

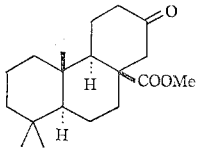
The structure and stereochemistry of atractyligenin, the aglycone of atractyloside, a toxic glucoside in the root of *Atractylis gummifera*, were substantiated as **158** by Melera *et al.*.[99]



(158)



(159)



(160)

Ireland *et al.*[100] synthesized, (±)-8β-methoxycarbonyl-13-oxopodocarpanone (as **160**), a degradation product of phyllocladene, through the Claisen rearrangement of compound **159** (represented as an enatiomer).

Ireland, Bell *et al.*[101] published a full paper of the total synthesis of (±)-kaurene and (±)-atisirene.

The courses of the syntheses are shown in Chart 11.

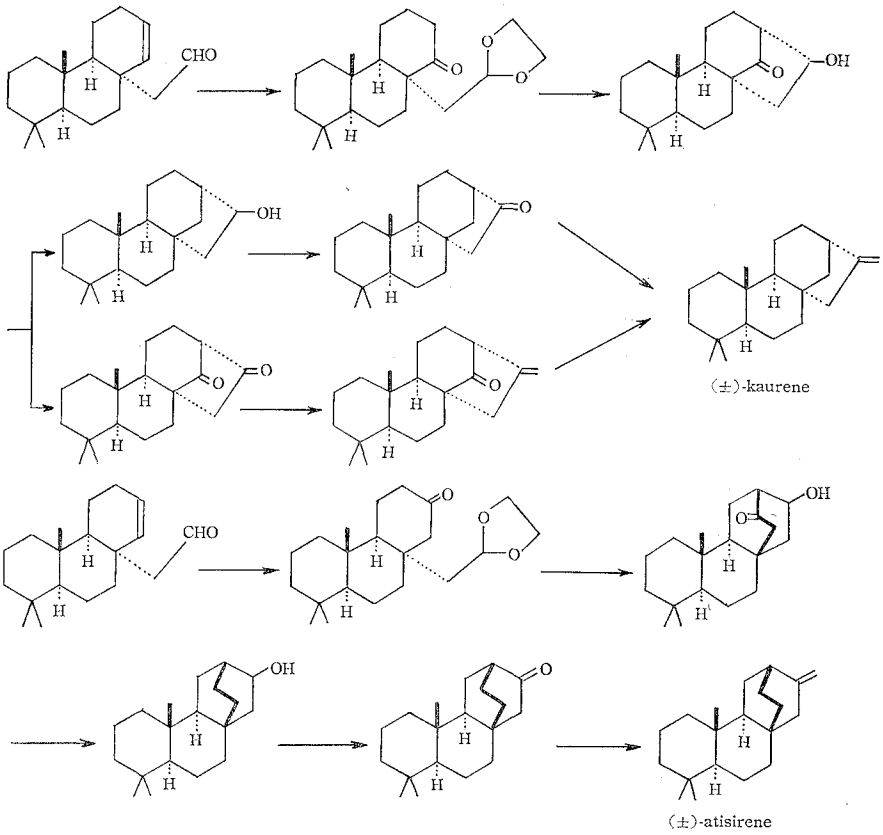


Chart 11

They[102] also published the full paper*5 of the total synthesis of (±)-hiabene. They described that the photosensitized oxidation of (±)-isokaurene and (±)-isoatisirene (as **155**) provides a pathway of the introduction of hydroxyl functions to these molecules, hence a pathway for a synthesis of the C-D rings system of diterpene alkaloid as shown in Chart 12.

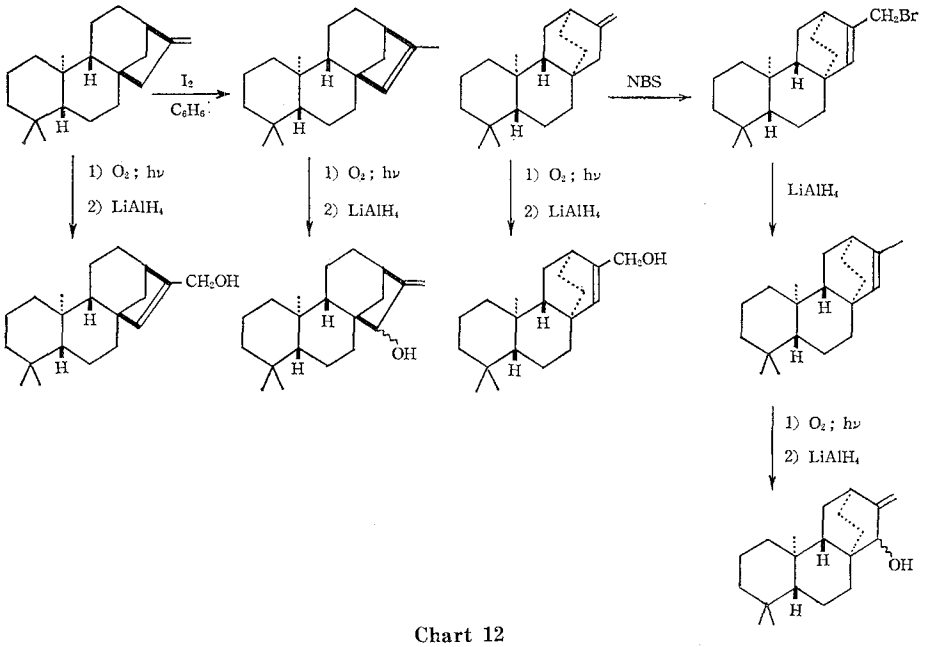
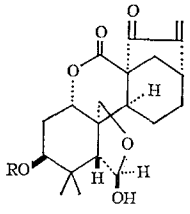
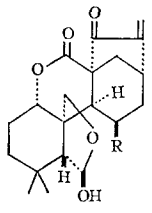


Chart 12

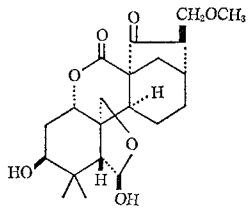
The total structure and stereochemistry of enmein **161**, a diterpene isolated from *Isodon trichocarpus* has been established,*6 and now, the full paper of the joint chemical work by two Japanese schools was published.[103]



(161) : R=H
(162) : R=Ac



(163) : R=H
(164) : R=OH



(165)

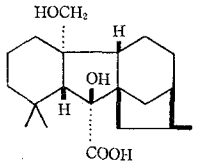
Fujita *et al.*[104] published a detailed full paper*7 on the chemical conversion of enmein (**161**) into (−)-kaurane, which confirmed the absolute configuration of enmein.

From *Isodon japonicus*, the pure enmein (not contaminated by dihydroenmein) and its 3-acetate (**162**) were isolated by Fujita *et al.*.[105]

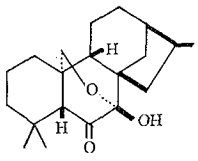
*5 For a preliminary report, see ref. 2. The course of the synthesis was shown in ref. 2.
*6 See ref. 1.
*7 For a preliminary communication, see ref. 2.

Subsequently, the same authors[106] reported the isolation of six new diterpenes, that is, isodocarpin, nodosin, isodotricin, trichodonin, ponicidin, and oridonon, and the structure elucidation of the former three diterpenes. On the basis of the spectral and chemical evidence, they presented the structure and absolute configuration **163**, **164**, and **165** for isodocarpin, nodosin, and isodotricin, respectively.

Okamoto *et al.*[107] presented a communication reporting a conversion of enmein into 4aα-hydroxymethyl-10β-hydroxy-1, 1, 8β-trimethylgibbane-10α-carboxylic acid (**166**). The compound was obtained in moderate yields, when 7-hemiketal-6-one **167** was heated in alkaline ethylene glycol. The alkali treatment of 7-hemiketal-6-ol **168** also yielded **166** conveniently. Compounds **167** and **168** were derived from enmein (**161**). Several attempts for removing the tertiary hydroxy group from **166** were tried.



(166)



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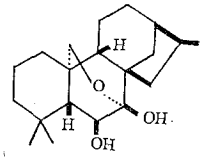
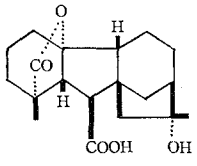


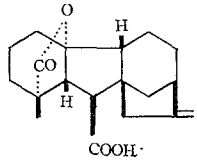
(168)

VI. GIBBANE AND ITS RELATED SKELETONS*8

Hanson[108] isolated gibberellin A_{10} from the culture filtrate of *Gibberella fujikuroi* and elucidated its structure as shown in formula **169**. The hydration of gibberellin A_9 (**170**) by standing in dil. hydrochloric acid for 68 hours at room temperature gave gibberellin A_{10} (**169**). During the course of this work 4b-epiallogibberic acid (**171**) was isolated from the fermentation.



(169)



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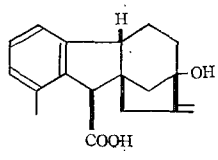

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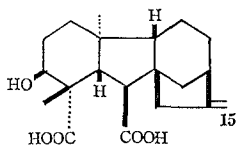
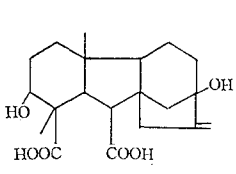


(172)
(183) ^{14}C at C-15

Cross[109] found that gibberellin A_{14}, a metabolite of *Gibberella fujikuroi*, is a new member of C_{20} gibberellins, and showed that its structure is **172**.



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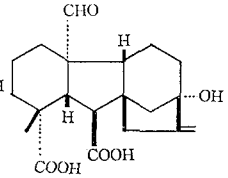

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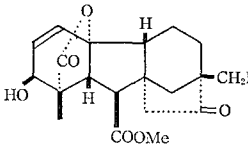

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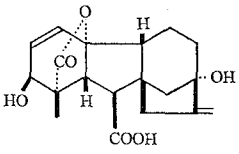


(176)

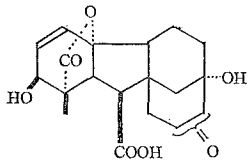
*8 See also section V, ref. 107.

Mitsui *et al.*[110] found a new C_{20} gibberellin which was named Lupinus gibberellin-I in immature seeds of *Lupinus luteus*, and proposed structure **173** for this new gibberellin.

Tamura *et al.*[111] isolated a new gibberellin which they called Bamboo Gibberellin from young bamboo shoot (*Phyllostachs edulis*) and proposed structure **174**.

Scott, Sim *et al.*[112] published a full paper describing an X-ray analysis of methyl bromogibberellate. They established the structure as **175**, hence the correct absolute stereochemistry of gibberellic acid was established as **176**.

Schreiber *et al.*[113] reported the epoxidation of gibberellins and a rearrangement of 8, 15-epoxide of gibberellic acid into a product (**177**) of ring-homoannulation in warm aqueous solution.



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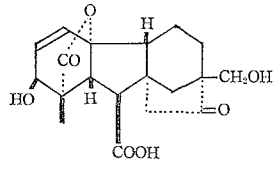

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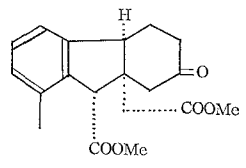
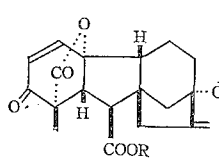


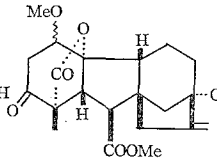
(179)

Girotra and Wendler[114] reinvestigated the foregoing rearrangement and recognized that the correct product is **178**. The structure of the latter was confirmed by its conversion into the known keto diester **179** through three steps of the reactions including epimerisations.

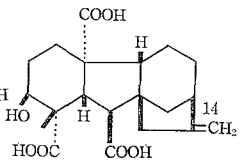
Kucherov *et al.*[115] treated methyl gibberellate with manganese dioxide in a dioxane-chloroform mixture for eighty hours and got 2-oxo derivative **180**. The same treatment of gibberellic acid itself yielded 3-oxo acid **181**. The latter was acetylated and kept one month in methanol to give **182** and its C-4 stereoisomer. Mainly, the former isomer was isolated from a similar treatment in a mixture of of methanol and acetic acid at reflux for 150 hours.



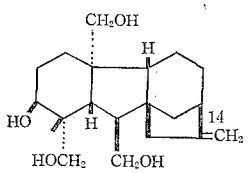
(180) : R=Me
(181) : R=H



(182)



(184)

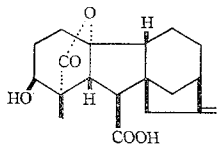


(185)

Cross and Norton[116] prepared [^{14}C]-gibberellin A_{14} (**183**) and added the latter into the fermentation of *Gibberella fujikuroi*. After three days, the isolated gibberellic acid and gibberellin A_{13} were found to be labelled with 4.7 and 0.9% incorporation, respectively. The authors prepared also [^{14}C]-gibberellin A_{13} (**184**) similarly and converted some of them into [^{14}C]-tetraol **185**. Both of them were neither incorporated by *Gibberella fujikuroi* into gibberellic acid, nor was tetraol converted into gibberellin A_{13}. The role of gibberellins A_{13} and A_{14} in the biosynthesis of gibberellic acid was discussed.

Geissmann *et al.*[117] studied on the biosynthesis of gibberellins from (−)-kaur-16-en-19-oic acid (**125**) and found that *Gibberella fujikuroi* utilizes **125** as a precursor

for the synthesis of gibberellins. A study of the time-course of the conversion of kaurenoic acid into gibberellins provided evidence that the sequence of steps involves an overall change toward higher oxidation levels, with gibberellins A_4 (**186**) and A_7 (**187**) at an earlier stage on the synthetic pathway than gibberellins A_1 (**188**) and A_3 (gibberellic acid (**176**)).



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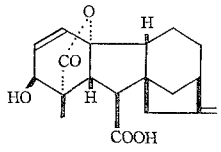

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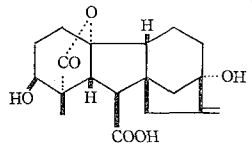
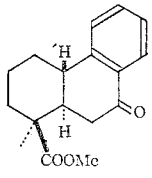
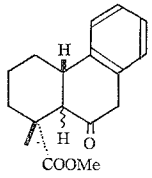


(188)

Matsui *et al.*[118] synthesized some resin acid analogues without angular methyl group, which may be used as the starting materials for the syntheses of gibberellins. The compounds are shown as formulas **189** to **192**.



(189)



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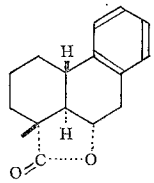

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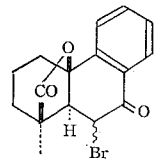
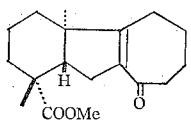
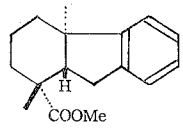


(192)

Bachi *et al.*[119] studied an approach to the synthesis of the ring A system of gibberellins from methoxynaphthoic acids.

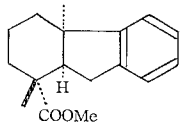


(193)

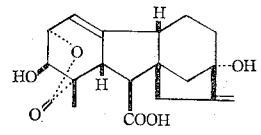


(194)

Tahara and Hoshino[120] gave a discussion on the synthesis of keto ester **193** which was regarded as a potential intermediate for the preparation of gibberellins.



(195)



(196)

The same authors[121] prepared *trans*-(**194**) and *cis*-(**195**) A/B ring fused isomer of 1α-methoxycarbonyl-1, 11α-dimethylhexahydrofluorene from abietic acid, and they converted **193** into **194** to confirm the structure of **194**.

Chatak and Chakravarty[122] tried acid-catalyzed cyclization of substituted benzylcyclohexanols and investigated the factors influencing the nature of cyclization products.

Mori[123] published a review on the structure and synthesis of the substances related to gibberellins giving 42 references.

Maheshwari and Bhalla[124] found the presence of at least three active gibberellin-like factors in the mature fruits of watermelon.

Spector and Phinney[125] described on the genetic control of gibberellin in *Gibberella fujikuroi*.

Grigoreva and Kucherov[126] published a review "Gibberellins".

Kucherov *et al.*[127] found the occurrence of a physiologically active isomer of gibberellic acid in the culture filtrate of *Fusarium moniliforme*. This compound corresponds to 2β, 3α, 7α-trihydroxy-1β-methyl-8-methylenegibb-4-ene-1α, 10β-dicarboxylic acid 1, 3-lactone (**196**).

Sciuchetti and Hutchison[128] discussed the influence of gibberellic acid and dimethylsulfoxide on the growth and metabolic products of *Datura tatula*.

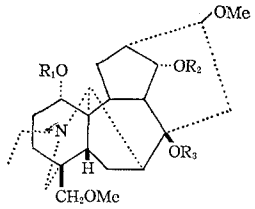
VII. DITERPENE ALKALOIDS*9

Clarke *et al.*[129] confirmed the configuration of C-13 and C-14 of cassaine (**93**) and that of C-7 of its related alkaloid, cassaidine (**94**).

Singh *et al.*[130] reported the isolation of two new alkaloids from *Aconitum falconeri*.

Kao *et al.*[131] isolated hypaconitine and five new alkaloids from *Aconitum koreanum*.

Pelletier *et al.*[132] studied the structures of condelphine, isotalatizidine, and talatizidine. They determined the location of their functional groups and the configuration at C-10 as shown. (condelphine : **197**, isotalatizidine : **198**, talatizidine : **199**)

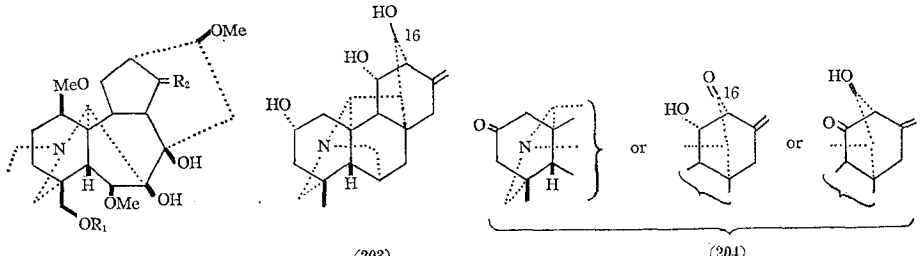


(197) : $R_1=R_3=H$, $R_2=Ac$

(198) : $R_1=R_2=R_3=H$

(199) : $R_1=R_2=R_3=H$ (β-OR_1)

Benn[133] isolated browniine (**200**), dehydrobrowniine (**201**), lycoctonine (**202**), hetisine (**203**), and a dehydrohetisine (**204**) from *Delphinium cardinale*. Delatine,



(203)

(204)

(200) : $R_1=Me$, $R_2=$

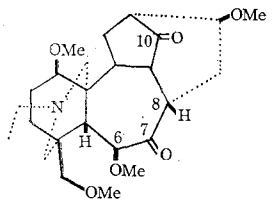
(201) : $R_1=Me$, $R_2=O$

(202) : $R_1=H$, $R_2=$

*9 See also section III, refs. 57-59.

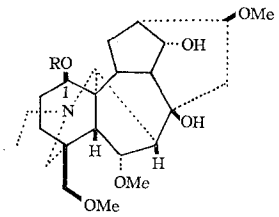
an alkaloid isolated previously from *D. elatum*, proved to be identical with hetisine. These are the first examples of the occurrence of hetisine, an *Aconitum* alkaloid, in *Delphinium* spp..

Marion, Edwards *et al.*[134] converted browniine (**200**) into 7, 15-seco-7, 10-diketone **205**, which proved to be identical with a product prepared by the isomerisation at C-6 from 7, 15-seco-7, 10-diketone **206** derived from chasmanine (**207**). The correlation confirmed the structure **207** tentatively assigned to chasmanine.[135]



(205)

(206) : α-OMe at C-6



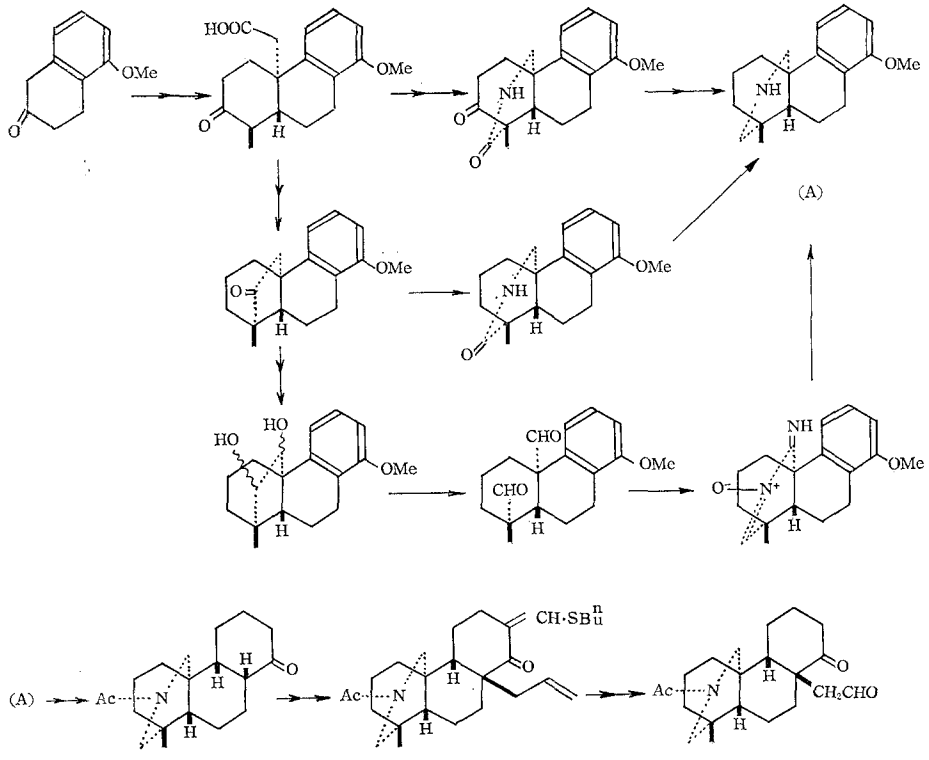
(207) : R=Me

(208) : R=H, α-OR at C-1

(209) : R=H

Marion *et al.*[136] revised the structure of neoline from **208** which was proposed by Wiesner *et al.*[137] to 1-O-demethylchasmanine itself (**209**), because the authors found that tri-O-methylneoline is identical with di-O-methylchasmanine.

Wiesner, Valenta *et al.*[138] published a full paper of their total syntheses of garryine, veatchine, and atisine. A preliminary communication was already described in my review.[1] The outline of the synthesis is shown in Chart 13.



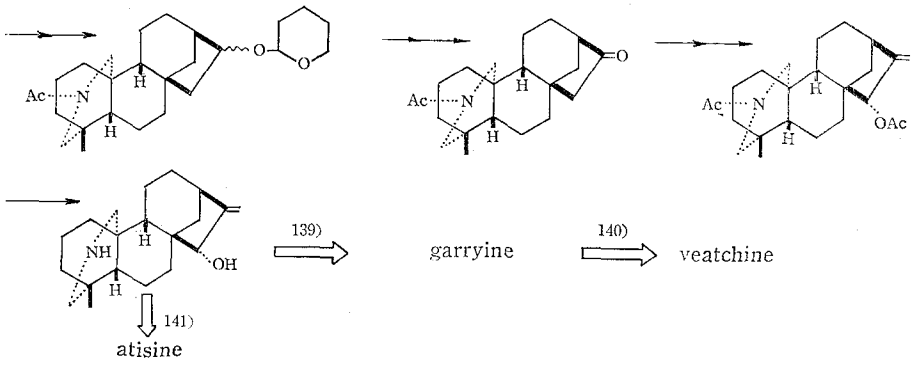


Chart 13

Subsequently, Tahara and Hirao[142] accomplished their total synthesis of garryine, veatchine, and atisine. Their route is shown in outline in Chart 14; their work is a synthesis of (−)-**210** from abietic acid which was already synthesized.

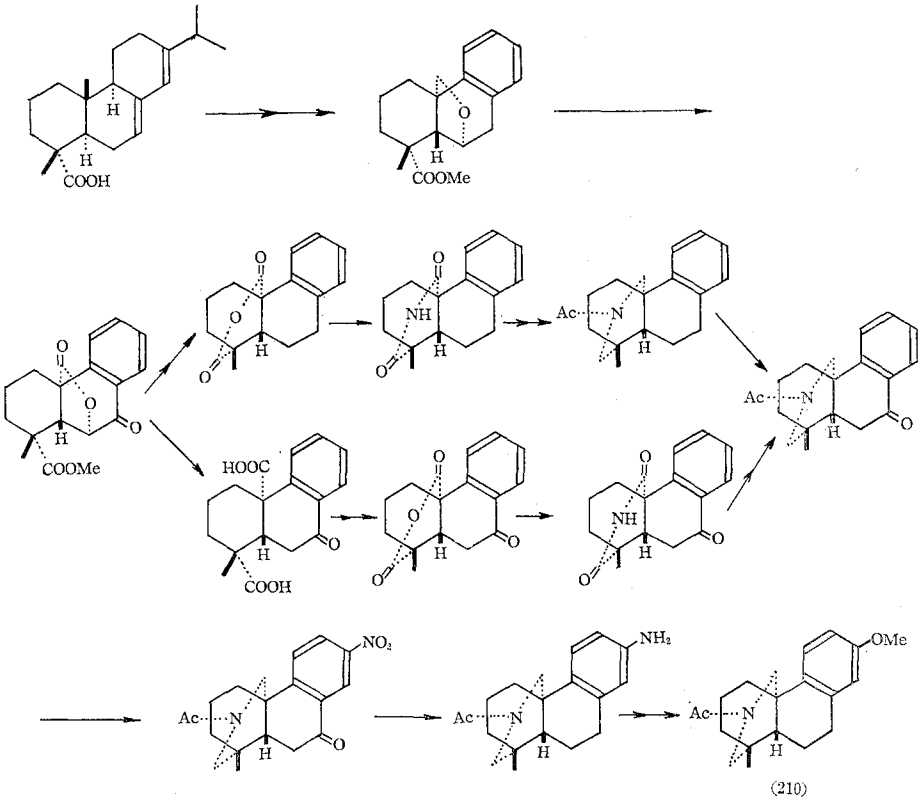


Chart 14

The authors compared the optical active product **210** with (±)-**210**, then carried out de-N-acetylation to (±)-**211**, which has been converted to (±)-atisine, (±)-veatchine, and (±)-garryine by Nagata *et al.*.[143] Thus, the route of the total synthesis was connected.

Wiesner and Philipp[144] synthesized compound **212** *via* several steps in an ap-

proach to songorine (**213**).

Wiesner, Valenta *et al.*[145] published another total synthesis of (±)-atisine. The outline of the route is shown in Chart 15.

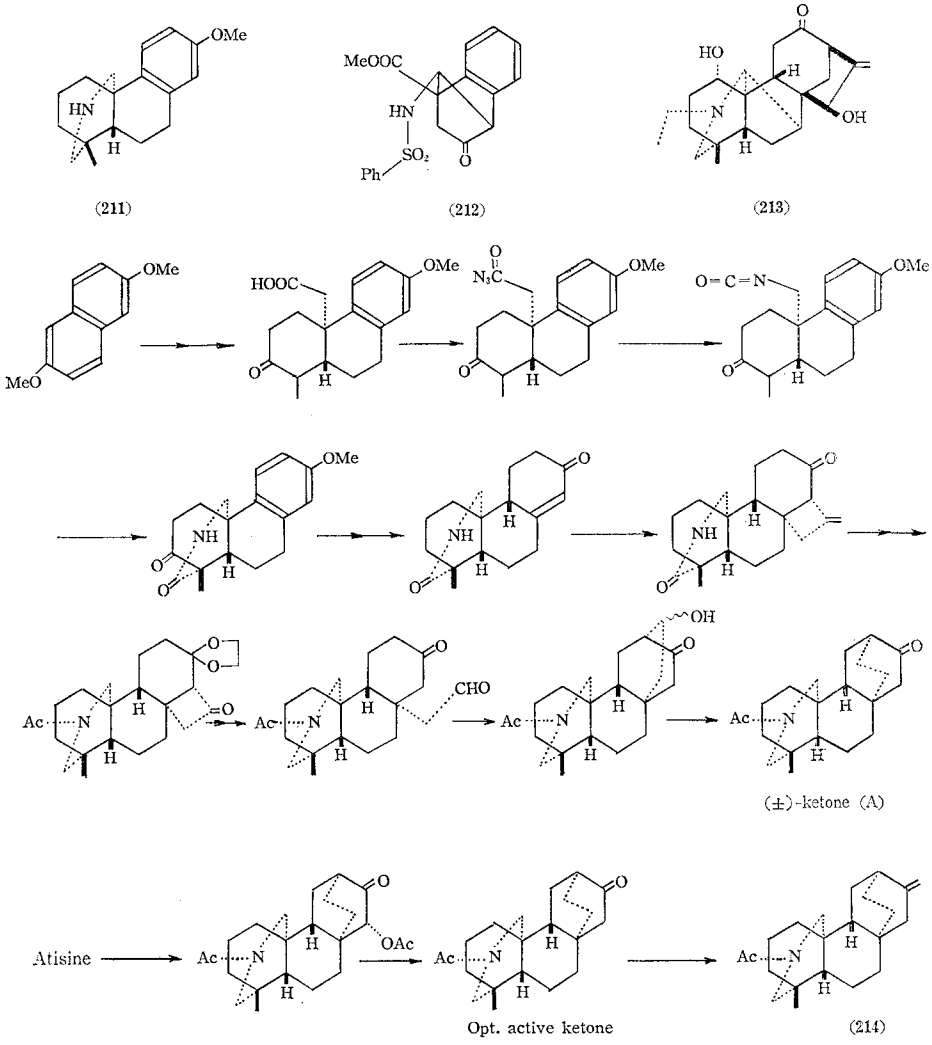
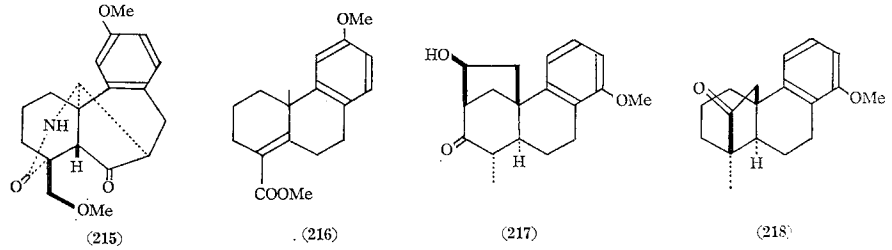


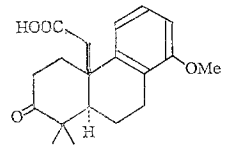
Chart 15

Since the conversion of **214** to atisine has already been described,[143,146,147] the preparation of (±)-ketone (A) represents a total synthesis of (±)-atisine.

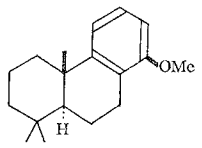


Wiesner and Santroch[148] synthesized compounds closely related to the aromatization products of aconitine and delphinine. One of them, for instance, is **215**.

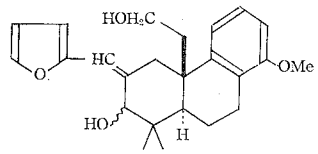
Turner *et al.*[149] described the syntheses of various intermediates—*e.g.* **216**, **217**, **218**, **219**, **220**, and **221**—related to diterpene alkaloids syntheses.



(219)

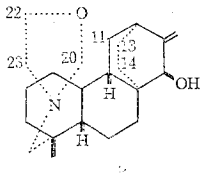


(220)

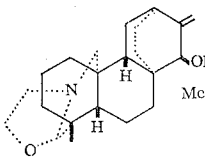


(221)

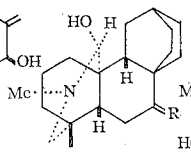
Pelletier *et al.*[150] described again that a big contribution of the driving force for atisine isomerisation (**222**→**223**) comes from the steric interaction among the hydrogens at C-20, C-13, and C-14, that is, the oxazolidine ring provides the major driving force for the isomerisation. Previously, Edwards *et al.*[151] suggested that the driving force for the isomerisation comes from the interaction of the ring oxygen with C-11 hydrogen. It was based on the isomerisation of **224**[151] and **225**[152] into the iso-compounds **226** and **227** by heating under reflux in methanolic alkali.



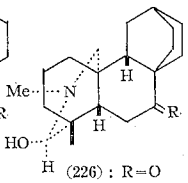
(222)



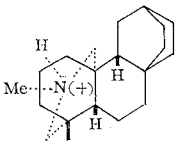
(223)



(224) : R=O
(225) : R=H$_2$



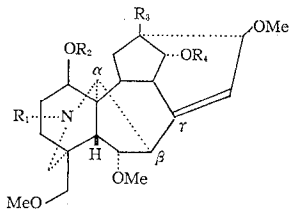
(226) : R=O
(227) : R=H$_2$



(228)

Pelletier *et al.* reinvestigated the treatment of **225** with 0.1 *N* methanolic alkali for 3.5 hours and found that the product was a mixture of the starting material **225**, iso-compound **227**, and a dihydro-compound **228**. So, they tried the isomerisation of atisine and **225** in methanol or ethanol without external base, that is, a comparison under the condition in which no reduction product was formed. In the case of the carbinolamine **225** no isomerisation could be detected after heating in methanol at 64° for seventeen hours or in ethanol at 78° for twenty hours, while pseudo first order rate-constant was obtained for the isomerisation of atisine.

Cookson *et al.*[153] studied a new type of chromophore. In the pyro derivatives (**229**-**232**) of the aconite alkaloids, the molecule is ideally set up for a σ-coupled transition; the electron pair on the nitrogen atom, the α, β bond, and the p orbital on Cγ are almost exactly in the same plane and parallel to one another. In fact, pyroneoline (**229**), pyrodelphonine (**230**), pyrochasmanine (**231**), and pyrobikha-



(229) : R_1=Et, R_2=H, R_3=H, R_4=H

(230) : R_1=Me, R_2=Me, R_3=OH, R_4=H

(231) : R_1=Et, R_2=Me, R_3=H, R_4=H

(232) : R_1=Et, R_2=Me, R_3=OH, R_4=H

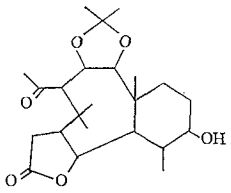
conine (232) all showed an unexpected absorption maximum at about 245 mμ (ε~6000), which was abolished by protonation of the nitrogen atom or amide formation.

VIII. THE OTHERS

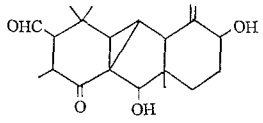
Bory *et al.*[154] investigated the reactions of diterpenic C-18 or C-19 esters with methyl lithium. The axial diterpene methyl esters yielded the methyl ketones, while the equatorial esters gave the mixtures of the corresponding tertiary alcohol and the methyl ketone. The sign of the Cotton effect of the methyl ketones thus obtained allowed to determine the absolute configuration of the original diterpene. Many kinds of the methyl ketones of the abietane, pimarane, and labdane types were prepared and their O.R.D. curves were determined.

Strizhakov[155] studied the mechanism of catalytic activity of acetic acid in rosin calcination. The formation of acetic anhydride followed by the reaction of the latter with a rosin acid gave a rosin acid anhydride, whose easy reaction with calcium oxide yielded calcium salt of the rosin acid.

Dried plants of *Marrubium peregrinum* were extracted with petroleum ether by a Russian group[156] and the extract, after removal of wax, was chromatographed on alumina. Ethereal eluate gave peregrinol, a diterpene. Subsequent extraction of the plant with acetone gave another diterpene, peregrinin.

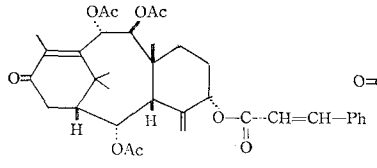


(233)

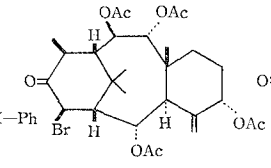


(234)

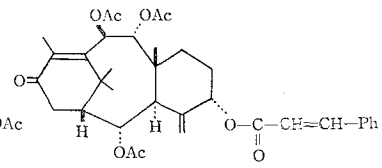
Uyeo *et al.*[157] elucidated the structure (233) of isopropylidenedihydrotaxinolactone, a byproduct which was formed in the treatment of dihydrotaxinol with acetone in the presence of *p*-toluenesulfonic acid or hydrochloric acid. The structure of anhydrotaxininol, a product in the treatment of taxinine with alcoholic sodium hydroxide, was already reported as a preliminary communication.[158] *[10] Now, the details of the experiments which allowed to assign structure 234 and discussions were published as a full paper by Uyeo *et al.*.[159]



(235)



(236)



(237)

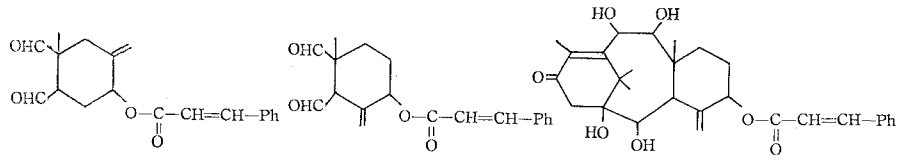
*[10] See also ref. 1.

In 1965, Nakanishi, Uyeo *et al.*[160] *11 proposed the stereostructure **235** for taxinine isolated from the leaves of *Taxus cuspidata*.

The X-ray analysis of 2, 5, 9, 10-tetra-O-acetyl-14-bromotaxinol by the same authors[161] established the stereochemistry of the compound as **236**, hence the stereochemistry of taxinine was revised to **237**, which resulted in a complete agreement with the conclusion by Lythgoe *et al.*.[162]

Nakanishi *et al.*[163] investigated and discussed the N.M.R. spectra determined with 60 and 100 Mc. on taxinine and its some derivatives.

Harrison and Lythgoe[164] revised structure **238** which was assigned[165] previously to the neutral dialdehyde fragment, a periodate cleavage product of O-cinnamoyltaxicin-I, to **239** on the basis of the N.M.R. investigations of its derivatives.

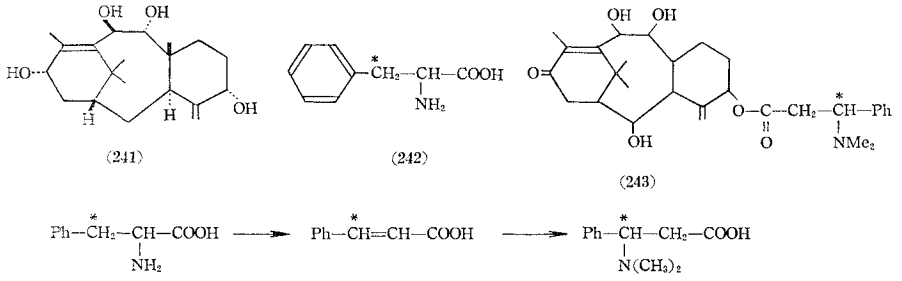


(238) 239) (240)

Subsequently, Lythgoe *et al.*[166] published a full paper establishing for O-cinnamoyltaxicin-I structure **240** which differs from a tentative earlier proposal[167] only in the position of the exocyclic methylene group.

Robertson *et al.*[168] established the structure of a new taxane derivative from the heartwood of *Taxus baccata* as **241** by the X-ray analysis of a *p*-bromobenzoate.

Leete and Bodem[169] fed DL-phenylalanine-3-^{14}C (**242**) to a third year *Taxus baccata*, and isolated taxine **243** after three weeks. After conversion of the radioactive taxine into taxinine (**237**), and hydrolysis, a radioactive cinnamic acid was oxidized to a radioactive benzoic acid, whose Schmidt reaction yielded an inactive aniline and an active carbon dioxide. Thus, the experimental results supported the biosynthetic scheme shown in Chart 16.



(241) (242) (243)

Chart 16

Pleuromutilin is an antibiotic inhibitory to gram-positive bacteria isolated from the Basidiomycetes *Pleurotus mutilus*, *P. Passeckerianus*, and *Drosophila subatrata*. Evidence was presented by Birch *et al.*[170] which confirmed the structure **244** for pleuromutilin. The specific incorporation of [^{14}C]-acetic and mevalonic acids as shown in Chart 17 verified its diterpenoid nature.

*11 See also ref. 2.

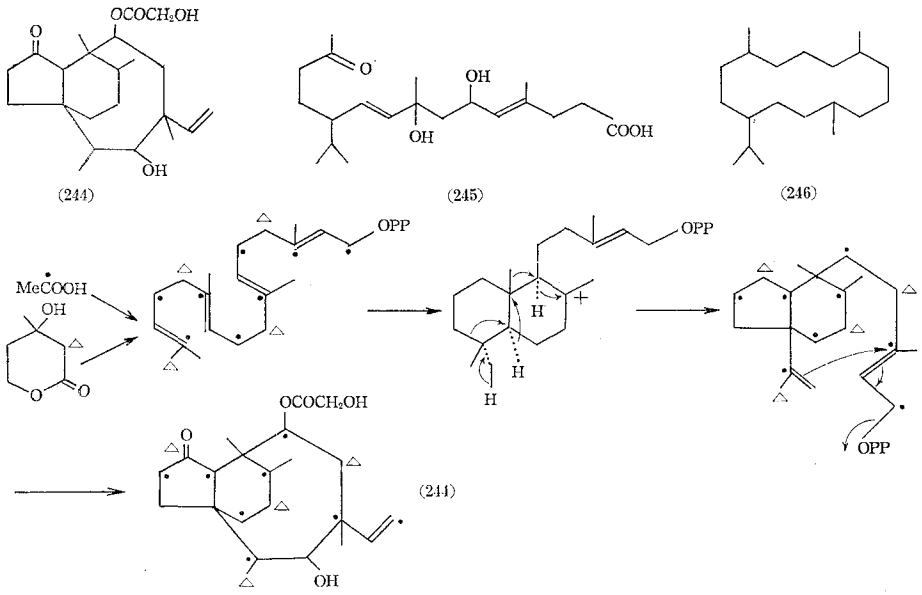


Chart 17

Two acyclic diterpenoid precursors of solanone were isolated from tobacco by Kinzer *et al.*,[171] and they were identified with the diastereoisomers of 6, 8-dihydroxy-11-isopropyl-4, 8-dimethyl-14-oxo-4, 9-pentadecadienoic acid (245).

Entwistle and Johnstone[172] synthesized cembrane (1, 5, 9-trimethyl-12-isopropyl-cyclotetradecane) (246). The route is shown in Chart 18.

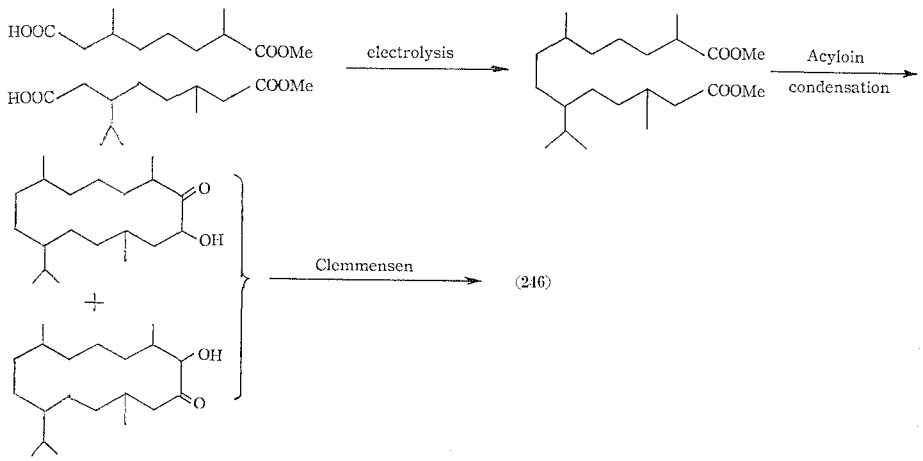
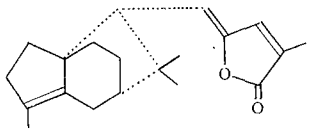


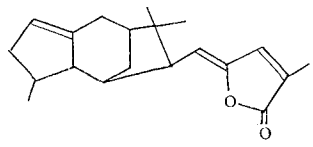
Chart 18

The X-ray analysis by Yow-lam Oh and Masien[173] established the structure and stereochemistry of iso-eremolactone as 247. Previously, Birch *et al.*[174] proposed structure 248 for eremolactone which had been isolated from *Eremophila freelingii*, and also presented structure 249 for iso-eremolactone, a bond isomerisation product of eremolactone. Now, they[175] reinvestigated their structure and presented some independent evidence supporting structure 247 for iso-eremolactone. Then,

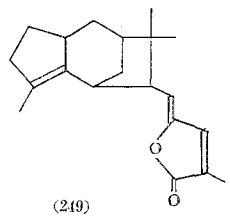
structure **250** was suggested for eremolactone.



(247)

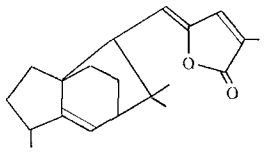


(248)

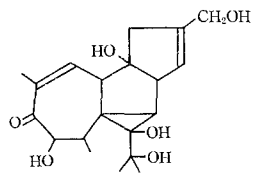


(249)

Hecker *et al.*[176] proposed structure **251** on the basis of the N.M.R. studies for phorbol isolated from *Croton* oil, and denied the structure presented by Arroyo and Holcomb.[177] *12



(250)



(251)

Finally, three reviews related to diterpenoids are shown. Sandermann[178] described the chemistry and biochemistry on the wood constituents. He wrote briefly on diterpenoids in his review.

Matsui and Mori[179] published a review on the chemistry of the plant hormones including gibberellins.

The same authors[180] introduced recent topics on the total synthesis of diterpenoid.

SUPPLEMENT

Enzell[181] *13 labelled podocarpa-8, 11, 13-triene derivatives with deuterium at positions, 1, 2, 3, 5, 6, 7, 11, 16, 17, and 20 and used them for mass spectrometric purposes. Clemmensen reduction was shown to provide a cheap and convenient way for reductive deuteration of ketones and aldehydes, and for the exchange of aromatic protons.

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*12 See also ref. 2.
*13 See ref. 24.

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