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Synthesis and Thermal Isomerization of Dictyopterene A and Related Compounds*

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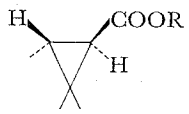
I. INTRODUCTION

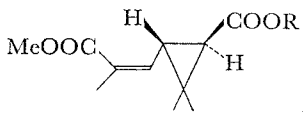
A number of aliphatic cyclopropane derivatives distribute widely in nature. Those which have been found so far are, for example, pyrethroids (**1**), lactobacillic acid (**2**), 1-aminocyclopropane-carboxylic acid (**3**) and so on. The flower heads of pyrethurum, *Chrysanthemum cinerariifolium,* contain six highly insecticidal esters which on complete hydrolysis, afford two kinds of cyclopropane-carboxylic acids, viz. chrysanthemic and chrysanthemum-dicarboxylic acids as acid moiety.[1] These six compounds may be represented by the general formula as follows:

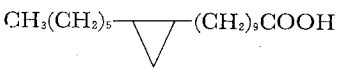


Pyrethroid

(**1**)

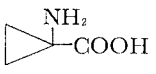
R: Cyclopentenolone moiety





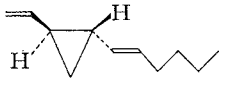
Lactobacillic acid

(**2**)



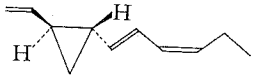
1-Amino cyclopropane carboxylic acid

(**3**)



Dictyopteren A
Moore *et al* (1968)

(**8**)



Dictyoptrene B
Moeore *et al* (1970)

(**9**)

The acid (**3**) has been isolated from perry pears.[2] Hypoglycins A (**4**) and B (**5**) are the constituents of unripe *Blighia sapida* fruits.[3] Sterculic (**6**) and malvalic acids (**7**) occur in the seed and leaf oils of the families, *Malvaceae* and *Sterculiaceae.* Malvalic acid usually predominates over sterculic acid with an exception in the seed oil of *Sterculia foetid.*[4]

* Taken from the dissertation (T. K.) submitted to Kyoto University (1971, April).

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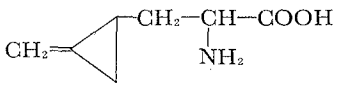
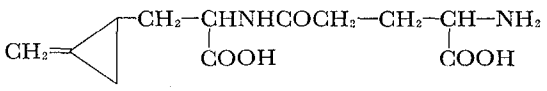
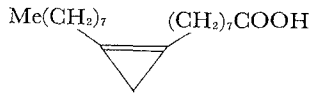


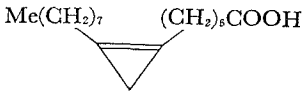
(4)



(5)



(6)



(7)

Because of the interest associated with the characteristic structure and physiological activity, many workers have long been engaged in the study of cyclopropane chemistry. In recent years, cyclopropane derivatives have aroused keen interest in particular from theoretical viewpoint of physical organic, synthetic chemistries as well as biosynthetic pathway, but there still remains much to be explored in this field of chemistry.

In 1968, Moore[5] isolated a novel hydrocarbon from the essential oil of fresh sea algae, *Dictyopteris polygamma* and *D. australis,* as the odoriferous constituent responsible for "ocean smell" and elucidated the structure as (+)-(*R* : *R*)-*trans*-1-(*trams*-1′-hexenyl)-2-vinyl-cyclopropane (**8**), and named dictyopterene A.

It was in 1970 that another hydrocarbon of the closely related structure, dictyopterene B, *trans*-1-(*trans, cis*-hexa-1′3′-dienyl)-2-vinylcyclopropane (**9**) was isolated by the same Hawaiian author from the same essential oil of the sea weed.[6] The reason why the synthesis of (±)-dictyopterene A (**8′**) attracted the present authors' attention is that (**8**) possesses in its side chain a *trans*-hexenyl group which might suggest some relation to leaf aldehyde, *trans*-2-hexene-1-al (**10**), which widely distributes in fresh green leaves of land plants and is looked upon as being a possible intermediate of the biosynthesis of terpenes with aroma.[7]

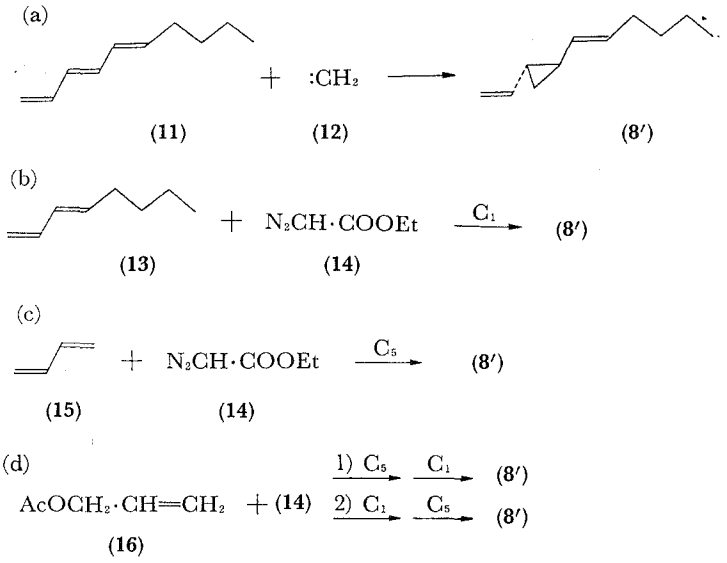
The synthesis of (±)-dictyopterene A (**8′**) was first achieved by Ohloff who obtained a mixture of the four possible stereoisomers of this compound, starting from butadiene and ethyl diazoacetate, and isolated the racemic isomer identical with the naturally derived hydrocarbon, by means of vpc with the synthetic mixture.[8]
The authors succeeded in the total synthesis of (±)-dictyopterene A (**8′**) by the synthetic scheme which will be described in details in the following chapters.

It is the advantage of the novel route of synthesis that sterically pure isomer can be obtained without contamination of the other isomers by more facile procedures and with a higher yield. This makes it easier to study cyclopropanoid chemistry and the authors were able to discuss reactivity, thermal isomerization and relation between steric structure and perfume of these compounds.

II. THE PRESENT RESEARCH

II-1 The strategy to approach to the synthesis of (±)-dictyopterene A (8′)

The authors present the following routes possible for achieving the whole architecture of dictyopterene A molecule, and is discussing the relative merits of the routes in comparison:



In the route a), one aims at one-step build-up of the C_{11}-skeleton of (**8′**) by adding a C_1-unit, methylene carbene (**12**), to a decatriene substrate (**11**), but it seems not feasible, since no methylene carbene has been known to selectively add only to the central C=C double bond of a conjugated triene, no matter what the carbene source and the reaction conditions may be. So that this may be reasonably rejected *a priori*. The second route b) consists of firstly forming a cyclopropane ring at the terminal ethylene of 1,3-octadiene (**13**) by the condensation of ethyl diazoacetate (**14**) and the subsequent transformation of the carboxyl group in the resulting cyclopropane carboxylate into vinyl group, say, by means of the Wittig vinylogation. In this case also, however, (**14**) can, by no means, discriminate between the two C=C double bonds and the condensation of diazoacetate would afford the C_{10}-cyclopropane products presumably in a variety of possible positional and stereochemical isomers, which obviously makes this route impractical for supplying enough materials to the succeeding vinylogation step. The third is that outlined and followed by Ohloff with success to ultimately obtain dictyopterene A (**8′**).[8] The first step in this synthesis resulted in the formation of a mixture of *cis*-, and *trans*-2-vinylcyclopropanecarboxylates as was expected and even with the separated *cis*- or *trans*-isomer, the subsequent Wittig olefin synthesis with a C_5-ylid afforded again two geometric side chain isomers of the desired dictyopterene A (**8′**). Difficulties with which these two isomers in the end products have to be isolated pure on vpc make this synthetic process inadequate for obtaining this compound in quantity, which is indispensable for the present authors to further elaborate the thermal rearrangement as well as olfactory chemistry of divinylcyclopropane systems.

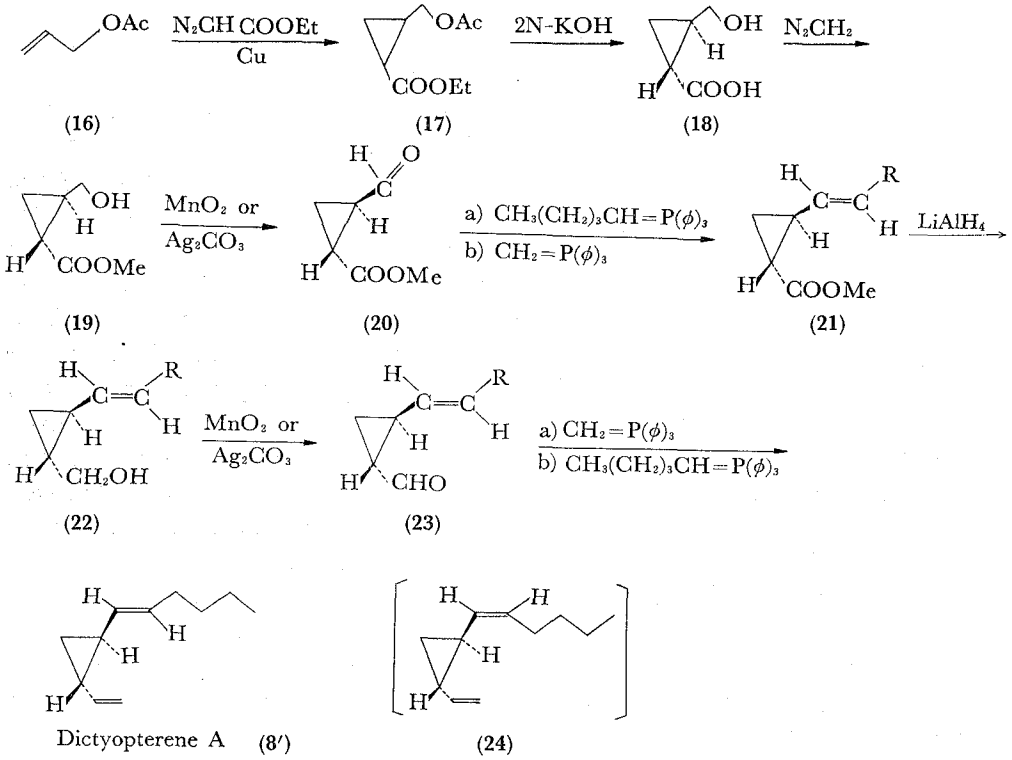
The last project d) seems the best to conform to the present authors' intention. In the first stage of this synthetic scheme, the addition of ethyl diazoacetate (**14**) to allyl acetate (**16**) would provide one with a *cis*, *trans*-mixture of the cyclopropane carboxylate, which after easy separation, could be subjected to the subsequent reactions of vinylogation (C_1) and olefination (C_5), thereby accomplishing the C_{11}-skeleton of (**8′**). In an alternative route, the second and the third steps may be inversed, *i.e.* one may

first lengthen the side chain by C_5 and thenafter by one methylene in order, both by means of the Wittig procedure.

The advantages of the present authors' process for the synthesis of dictyopterene A over the other routes a-c will be apparent and self-explanatory as one comes to the following chapter describing in details the discussion of the experimental results.

II-2 Synthesis of (±)-Dictyopterene A (8′)

In the first step of the scheme, the copper-catalyzed condensation of ethyl diazoacetate (**14**) with allyl acetate (**16**), a precaution was exercised to avoid the self-condensation of (**14**), where a large excess of (**16**) was employed. The reaction product thus obtained still contained some impurities such as methyl maleate and was then purified by permanganate oxidation to remove olefinic contaminants. The alkaline hydrolysis gave *trans*-2-hydroxymethylcyclopropanecarboxylic acid (**18**) after repeated recrystallizations, m.p. 64–5°. This was esterified with diazomethane by the standard method into the methyl-ester (**19**), the purity of which was again evidenced by the sharp single peak in vpc.



Exploratory oxidations of (**19**) were carried out with use of various oxidizing agents such as MnO_2, Ag_2CO_3, DMSO, CrO_3, K_2CrO_7 and *tert*-butyl chromate, under the specified conditions respectively, and among them manganese dioxide and silver carbonate were found to be the oxidants of choice in this case of cyclopropane-alcohol (**19**). Thus, the cyclopropyl carbinol (**19**) was shaken with active manganese dioxide, carefully prepared from manganese sulfate and sodium hydroxide, in dry ether. The

yield of the oxidation product, methyl 2-formyl-cyclopropanecarboxylate (**20**) was satisfactorily good (80%).

In an alternative way, the carbinol (**19**) in benzene was oxidized with silver carbonate under reflux and simultaneously removing water formed by azeotropic distillation. The fractional distillation of the reaction product yielded the desired cyclopropylcarboxyaldehyde (**20**) in a good yield (80%). It therefore appears that the employment of silver carbonate is recommendable to the oxidation of cyclopropylcarbinol without affecting the carbalkoxy group.

The consecutive vinylogations of the cyclopropane carboxyaldehyde (**20**) by means of the Wittig technique will lead to the ultimate structure of dictyopterene A. As was mentioned in the strategy, two routes are conceivable for this approach, *i.e.* in the first A, the reaction of the cyclopropane carboxyaldehyde (**20**) with *n*-pentylidenetriphenylphosphorane was carried out in the standard manner to give methyl *trans*-(1′-hexenyl)-cyclopropanecarboxylate (**21**). The vpc analysis of the reaction product obtained revealed that it consisted of a mixture of *cis*- and *trans*-1′-hexenyl side chain isomers in a ratio of 95 : 5, the former being the undesired isomer. Even by the *trans*-selective procedure of the Wittig reaction devised by Schloser and Corey, the formation of the *cis*-1′-hexenyl isomer amounted to 60% of the product. In the improved procedure as applied to the aldehyde (**20**), pentylidenetriphenylphosphorane was prepared at 20°C from pentyltriphenylphosphonium bromide and butyl lithium and to this ylid was introduced the aldehyde (**20**) at −40°C. Then, more butyl lithium was added to shift the equilibrium between *cis*- and *trans*- betaine intermediates towards the stable *trans*-side, and finally the reaction mixture was quenched by adding *t*-butylate to yield the olefin end-product in favor of the *trans*-isomer. This resulted actually in an unsatisfactory yield of the desired *trans*-side chain isomer (*vide supra*) and consequently, this route A seemed not promising for further process, although the transformation and vinylogation of this compound ultimately reached dictyopterene A.

Then the authors preferred the alternative route B to the above-mentioned A with the Corey modification. As will become apparent later, the route B is more advantageous over the former in assuring a stereoselective synthesis of the *trans*-side-chain isomer. The preferred process followed the first vinylogation by one carbon of the aldehyde intermediate (**20**) and the subsequent appropriate chemical transformation so as to be capable of undergoing the second Wittig reaction, by which a pentenylation is effected to lead to the final product hydrocarbon. In practice of this synthetic route, methylenetriphenylphosphorane was allowed to react with the cyclopropane-carboxyaldehyde (**20**) in usual way to afford methyl *trans*-2-vinyl-cyclopropane-carboxylate (**21**-b) in a satisfactory yield (80%). This, of course, lacks geometrical isomerism in the side chain and therefore, as such was able to be subjected to further transformations. The vinylcyclopropane ester (**21**-b) was reduced with $LiAlH_4$ to the corresponding carbinol, *trans*-2-hydroxymethyl-vinylcyclopropane (**22**-b), which in turn, was converted into the formyl-derivative, *trans*-2-formyl-vinyl-cyclopropane (**23**-b) by means of the unique method of oxidation devised by the present authors. Another Wittig vinylogation by 5 carbons of the C_6-cyclopropane carboxyaldehyde (**23**-b) with pentylidenetriphenylphosphorane accomplished the construction of the whole architecture of dictyopterene A molecule (**8′**). The final product hydrocarbon thus

obtained, (±)-*trans*-2-(*trans*-1′-hexenyl)-vinylcyclopropane (**8′**), was found to be identical in all respects with that previously obtained via the route A, as well as the naturally derived (+)-dictyopterene A (**8**), except the rotation. It was suprising that the final product via this route B was practically free from the contamination of the *cis*-side chain isomer as evidenced by vpc, NMR and IR analyses. It then follows that the present authors' route of synthesis provides one with the stereospecific synthesis of (±)-dictyopterene A and the related analogues, in satisfactory over-all yield.

The identity of the synthetic specimen with the naturally occurring dictyopterene A (**8**) was obtained and undoubtedly evidenced by the comparison of IR-, NMR-, and MAS-spectra of the author's specimen with those, supplied by Dr. Moore, of (+)-dictyopterene A (**8**). Furthermore, the inspection of the spectra fully substantiated the proposed structure.

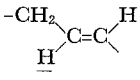
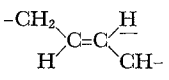
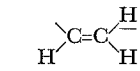
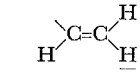
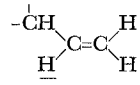
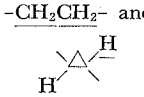
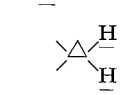
IR-spectra:

The IR-spectra of the synthetic specimens (**8′**) and (**24**) showed very strong bands at 1640 cm^{-1}, 980 cm^{-1} and 893 cm^{-1}, attributable to a vinyl group. In addition to the main absorption, a number of characteristic bands of (**8′**) were identical with those of (**24**), except the disubstituted *trans*-ethylene at 958 cm^{-1}.

NMR-spectra:

The NMR-spectral data are summarized in Table I.

Table 1. NMR Spectral Data of Dictyopterene A

Description of signal	No. of protons	Chemical shift	Coupling constant	Assignment
Broad quartet	2	1.95	7	$-CH_2\underline{CH_2}CH=$
Doublet of triplets	1	5.45	15.5, 7	
Doublet of doublets of triplets	1	4.99	15.5, 6, 1.2	
Doublet of doublets	1	4.98	17, 2.5	
Doublet of doublets	1	4.81	10, 2.5	
Doublet of doublets	1	5.37	17, 10, 6	
Triplet	3	0.77	7	$CH_3\underline{CH_2}-$
Multiplet	6	ca. 1.25		$-\underline{CH_2CH_2}-$ and 
Triplet	2	0.87	7	

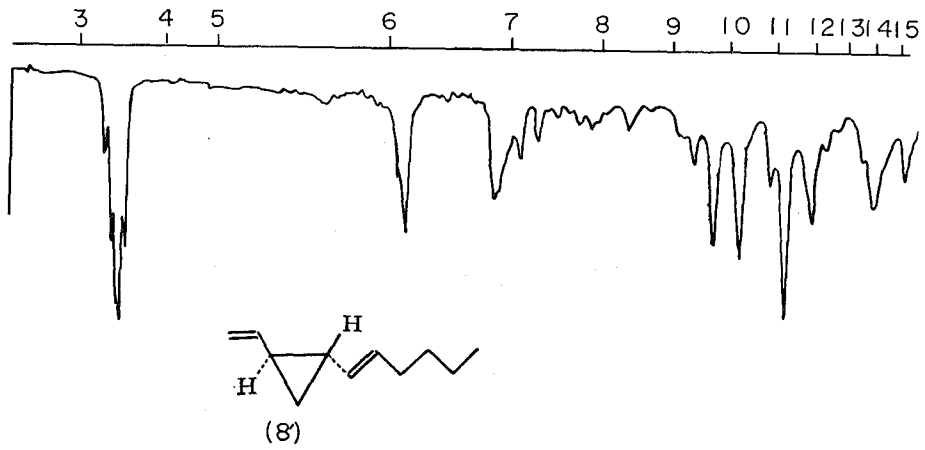

3 4 5 6 7 8 9 10 11 12 13 14 15
H
H
(8')

Fig. 1.

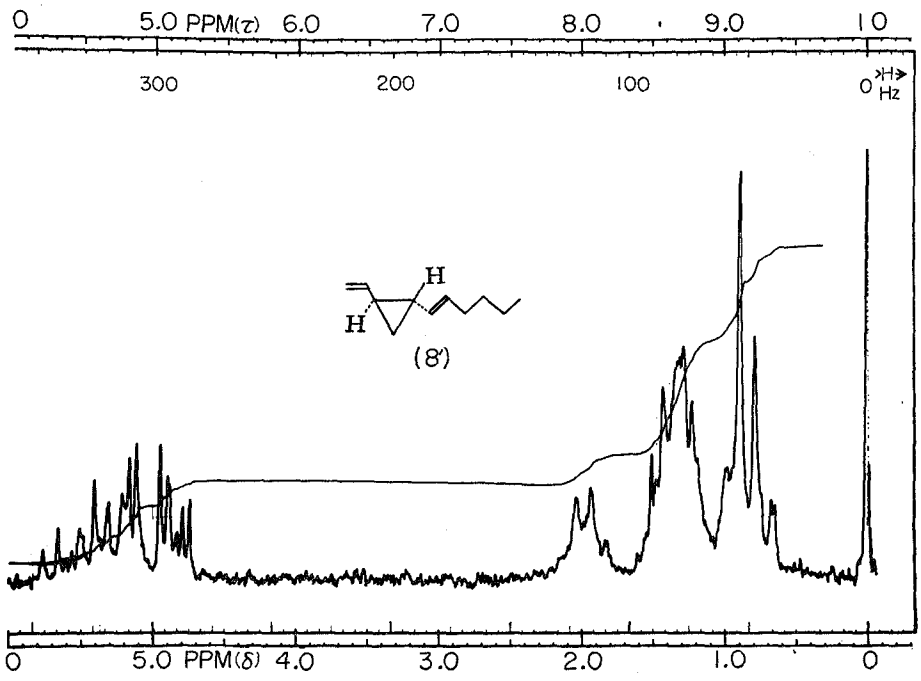

0 5.0 PPM(τ) 6.0 7.0 8.0 9.0 10
300 200 100 0 Hz
H
H
(8')
0 5.0 PPM(δ) 4.0 3.0 2.0 1.0 0

Fig. 2.

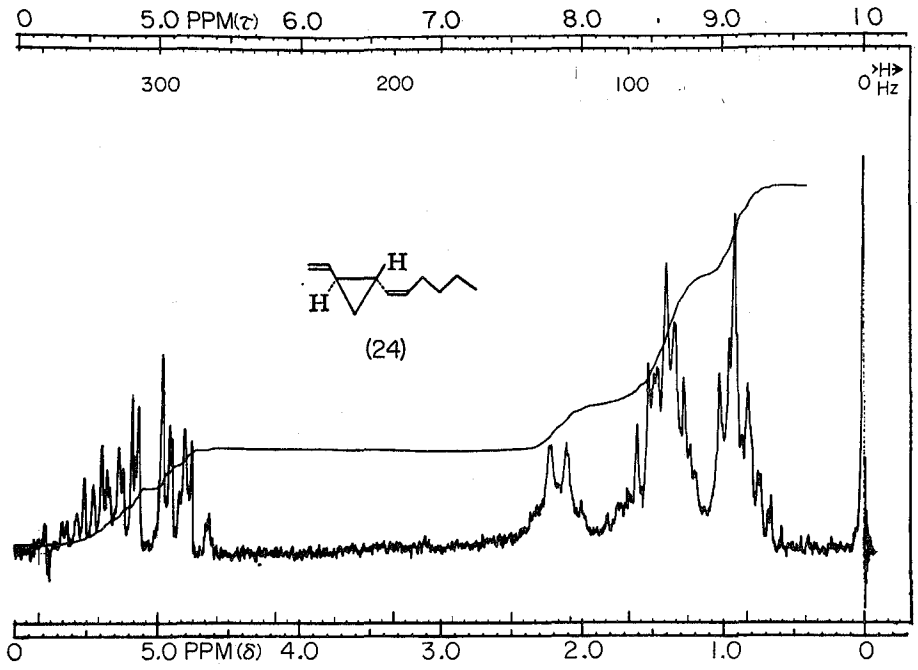

0
5.0 PPM(τ)
6.0
7.0
8.0
9.0
10
300
200
100
0 Hz
H
H
(24)
0
5.0 PPM(δ)
4.0
3.0
2.0
1.0
0

Fig. 3.

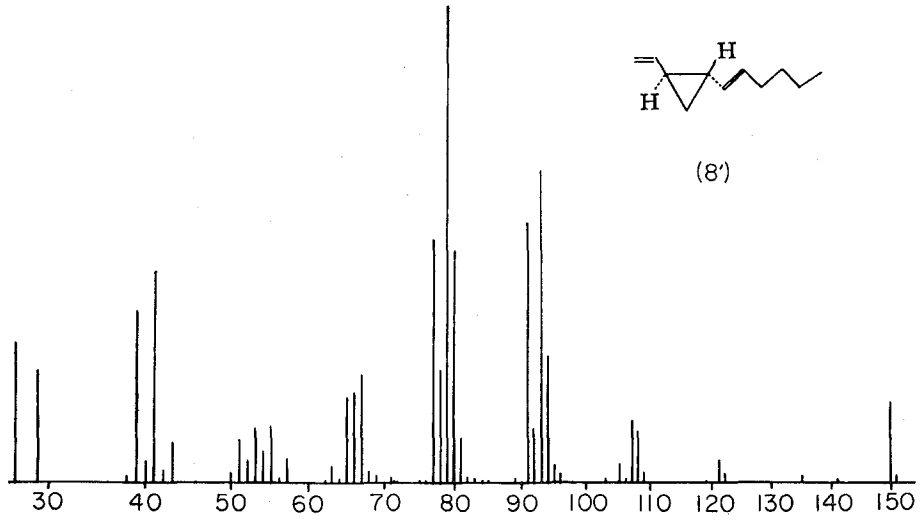

H
H
(8')
30
40
50
60
70
80
90
100
110
120
130
140
150

Fig. 4.

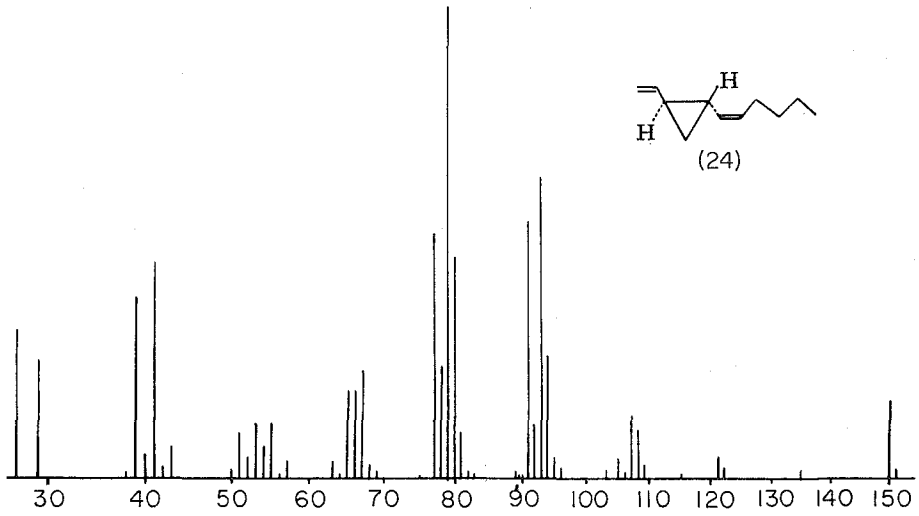
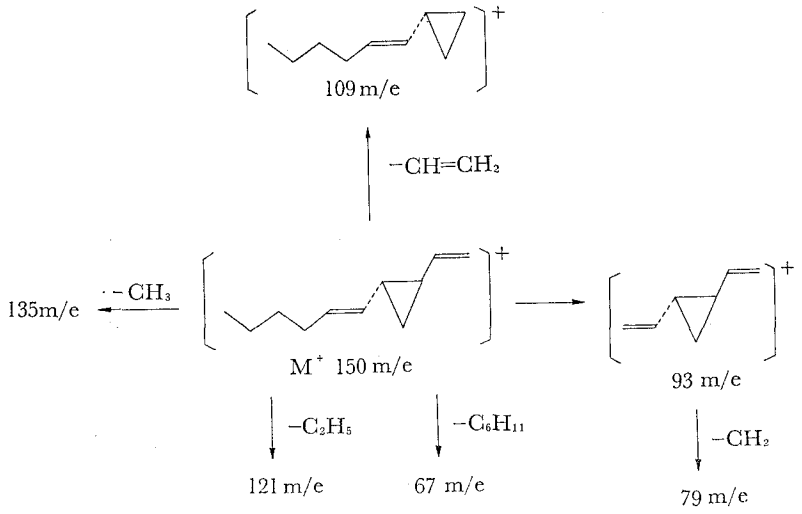


Fig. 5.

MAS-spectra:

As can be seen from the charts and the tabulated data, the MAS-spectra of (**8′**) were nearly identical with that of (**24**).

The loss of C_4H_9 and CH_2 from the molecular ion leads to the base peak (at 79 m/e) of both spectra. The fragmentation scheme for the synthetic dictyopterene A was proposed below.



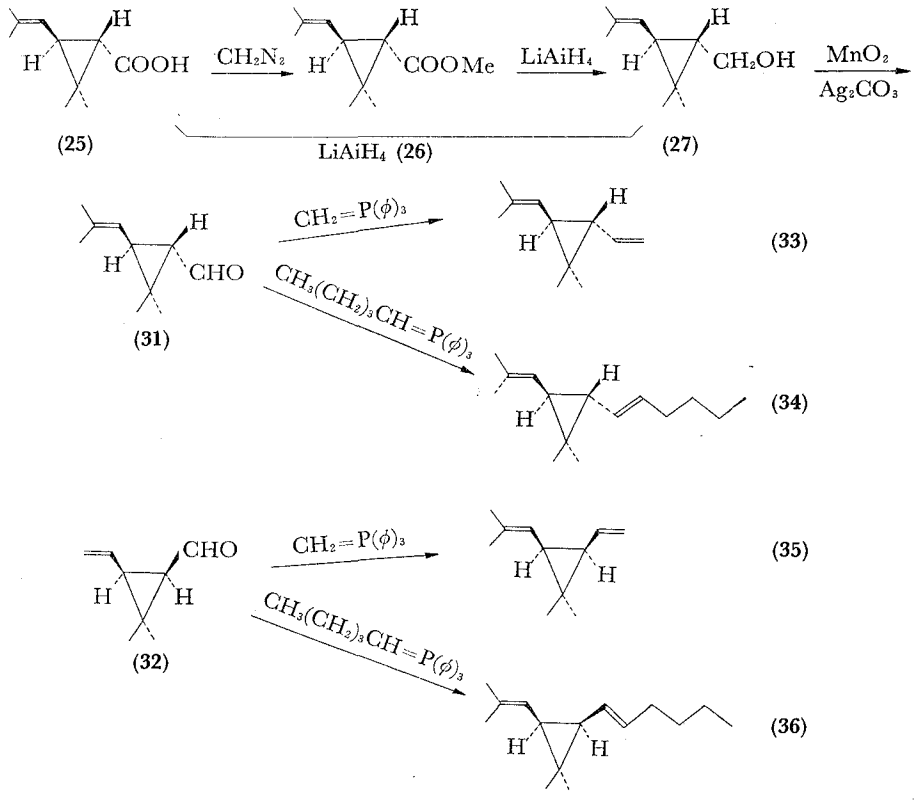
II-3 Synthesis of the related compounds

Synthesis of the divinylcyclopropane derivatives analogous to dictyopterene A would certainly be informative in revealing the relationship between odor and chemical structure and elucidating the thermal and photochemical behaviors of divinylcyclo-

propanes. It seemed interesting to note that by applying the same synthetic techniques and the same reagent which had been used with success in the synthesis of dictyopterene A, one could obtain some divinylcyclopropane analogs starting from *cis*-(**28**) and *trans*-chrysanthemic acids (**25**). Chrysanthemic acid is a C_{10}-terpene acid of a substituted mono-vinylcyclopropane with a potential functional group (carboxyl) capable of undergoing the Wittig vinylogation. In addition, this compound has an advantage of the well-defined geometry of the cyclopropane ring and serves well as the starting material because of its easy accessibility. Those which have been derived from isomeric chrysanthemic acids (**33**), (**34**), (**35**), and (**36**), the synthetic schemes of which are shown below.

In addition to these, *cis*-2-acetyl-vinylcyclopropane (**42**), the simplest oxygen analog of divinylcyclopropane, was also synthesized by the following process. This synthesis stemed from the authors' intention to explore the thermal sigmatropic behavior of the oxygen analog in comparison with those of divinylcyclopropanes.

The synthetic process may be illustrated by *trans*-3,3-dimethyl-2-vinylisobutenyl-cyclopropane (**33**). *trans*-Chrysanthemic acid (**25**) was first converted by $LiAlH_4$ reduction into *trans*-chrysanthemol (**27**). This reduction was easily effected in the present author's procedure (see experimental), in spite of Crombie's claim that this was not feasible when he started from free chrysanthemic acid. It depends on the reaction conditions and particularly on the quantity of the reagent used whether or not this procedure successfully affords chrysanthemol.



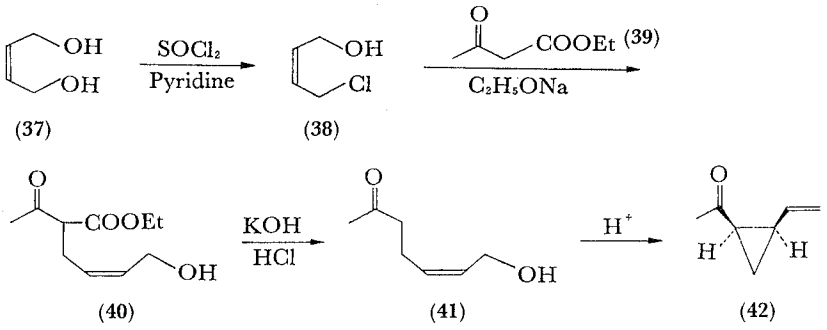
The subsequent oxidation of chrysanthemol (**27**) into chrysanthemal (**31**) was carried out in exactly the same way as in the case of dictyopterene A (**8′**) which was described earlier.

The vinylogation of chrysanthemal (**31**) with methylene-triphenylphosphorane by the Wittig technique, also as mentioned above, finally afforded *trans*-3,3-dimethyl-2-vinyl-*iso*butenylcyclopropane (**33**), whereas with another ylid in *n*-penthylidene-triphenylphosphorane, chrysanthemal (**31**) gave *trans*-3,3-dimethyl-2-(*trans*-1′-hexenyl)-*iso*butenylcyclopropane (**34**).

The same procedure with the isomeric *cis*-chrysanthemol (**30**), equally furnished the corresponding divinylcyclopropane derivatives, *cis*-3,3-dimethyl-2-*iso*butenylvinyl-cyclopropane (**35**) and *cis*-3,3-dimethyl-2-(*trans*-1′-hexenyl)-*iso*butenylcyclopropane (**36**).

It is worthy of note that in the cases of (**34**) and (**36**), the Wittig reaction proceeded in a stereoselective manner as to afford the *trans*-isomer alone, as was the case with dictyopterene A.

The oxygen analog of divinylcyclopropane system, *cis*-acetylvinylcyclopropane (**42**), was obtained by the sodium ethylate-catalyzed condensation of 4-chloro-*cis*-2-butene-1-ol (**38**), involving the intermediate formation of hydroxy-2-heptene-6-one (**41**), which upon distillation in the presence of acid catalyst, eventually afforded the desired product (**42**). The identity was confirmed by IR, NMR, MAS, and vpc means.



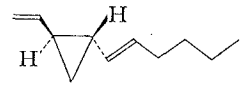
II-4 Odor of the divinylcyclopropanes

Little has been known on the mechanism of olfaction as well as on the relation between chemical structure and odor. However, only one mechanism of olfaction has been proposed: The hypothesis states that low-frequencey vibrations or rotations provide the physical basis of odor. This hypothesis accounts well for the failure of chemists of find correlations between odor and chemical constitution, because unlike a purely chemical theory, it looks on the molecule primarily as a mechanical system of mass points and elastic forces.[9]

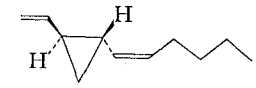
It is quite the case with the present system of divinylcyclopropane derivatives and it seems very difficult or almost impossible to deduce any relationship between chemical structure and odor of compounds of divinylcyclopropane type, since the variety of compounds to be subjected to olfactory panel tests are too scarce. However they still

permit one to draw a qualitative tendency of stereochemistry responsible for the special sort of smell.

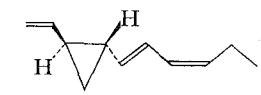
Moore described that naturally derived (+)-dictyopterene A (**8**) possesses an odor reminiscent of the "ocean smell", but this compound alone can not reproduce the whole flavor of algae. The algae flavor consists of dictyopterene A (**8**) and B (**9**) and *trans, cis, cis*-undecatetraene (**43**) which may probably be the biogenetic precursor of A (**8**) and other terpenes. The mixture of dictyopterene A (**8'**) obtained in the present synthesis and dimethylsulfide gave an odor like laver at very low concentrations. *cis*-(**35**) and *trans*-3,3-dimethyl-2-vinyl-*iso*butenylcyclopropane (**33**) also have an odor like edodes, whereas *cis*-(**36**) and *trans*-3,3-dimethyl-2-(*trans*-1'-hexenyl)-*iso*butenyl-cyclopropane (**34**) make one recall lichen.



(**8**)

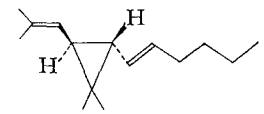


(**24**)

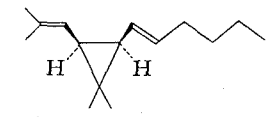


(**9**)

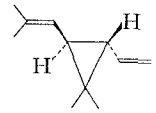
(**43**)



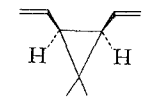
(**34**)



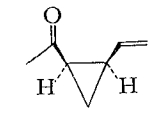
(**36**)



(**33**)



(**35**)

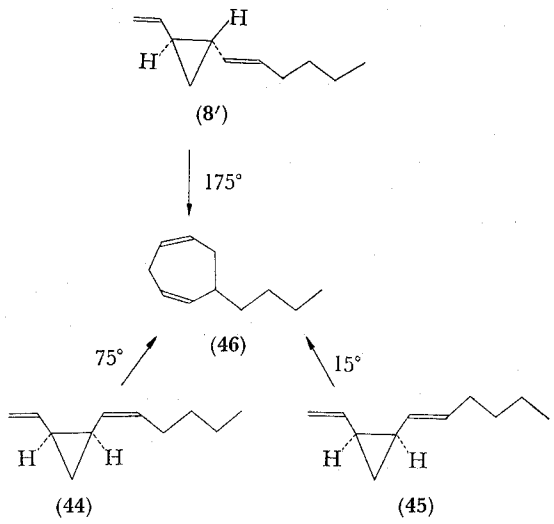


(**42**)

In a qualitative olfactory test, the odor of (**33**) is more intense than that of (**35**). It is apparent that the difference in intensity of odor is based on the steric factor about the cyclopropan ring, since both (**33**) and (**35**) are constitutionally equal in every respect except the geometry of cyclopropane ring. This was further confirmed by the comparison of (**34**) and (**36**), where the *cis*-isomer (**36**) is less intense in odor than the *trans*-(**34**). As regards the side chain geometry in the synthetic dictyopterenes, *trans*-2-(*trans*-1'-hexenyl)-vinylcyclopropane (**8'**) is stronger in olfactory sense than the corresponding side chain *cis*-isomer (**24**), showing that the odor of this type of compounds is significantly affected also by the geometrical configuration of the side chain.

II-5 Thermal isomerization of divinyl-cyclopropanes

In Vogel's mechanism,[10] the difference in reactivity between *cis*- and *trans*-divinylcyclopropanes can be reasonably understood, but the reactivity difference between the alkylated and non-alkylated divinylcyclopropanes is not explained satisfactorily. It was in an attempt to resolve this difficulty that the present authors have synthesized a few alkylated divinylcyclopropane (**8'**) and (**35**). In addition, the simplest oxygen analog, *cis*-2-acetylvinylcyclopropane (**42**), underwent a thermal isomerization to give cyclopentene derivative, instead of the expected oxepine derivative.



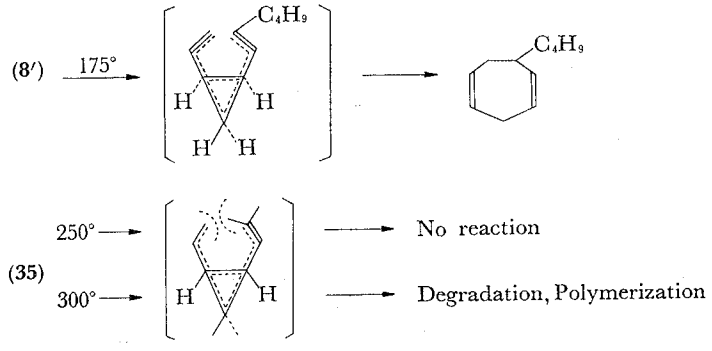
Pyrolysis of these divinyl derivatives was conducted in a sealed tube under reduced pressure at/or below 0.1 mmHg at appropriate temperatures.

Even at −40°C, *cis*-divinylcyclopropane isomerized to give *cis*, *cis*-cycloheptadiene, but alkylated divinylcyclopropane, for example, *cis*-2-hexenylvinylcyclopropane was recovered unchanged after the same treatment.

In view of the electronic theory, this result are not reasonably understood, because it may be considered that alkylated vinylcyclopropane should be more reactive than the corresponding non-alkylated compounds.

Furthermore, the thermolysis of *cis*-2-(*trans*-1′-hexenyl)-vinylcyclopropane (**45**) at 15°C yielded the corresponding heptadiene, whereas in *cis*-2-(*cis*-1′-hexenyl)-vinylcyclopropane (**44**), heating up to 75°C was necessary to effect the rearrangement to the same 7-membered ring. Based on these facts, the authors deduced that the steric requirement of a quasi-boat conformation with the two substituents faced to each other in the transition state must be fulfilled for this system to undergo a sigmatropic rearrangement to form a seven-membered ring. In this case, therefore, it seems likely that alkylated divinylcyclopropanes do not meet the steric requirements because of its steric hindrance exerted by alkyl groups, thus making the compound less reactive.

To confirm this hypothesis, *cis*-3,3-dimethyl-2-vinyl-*iso*-butenylcyclopropane

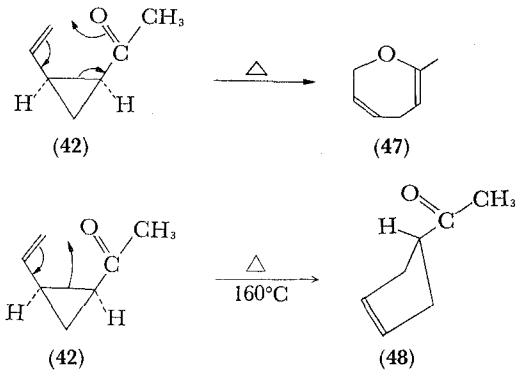


(**35**) was treated at an elevated temperature (200–250°C) under a reduced pressure, but this was recovered unchanged.

The pyrolysis of (**35**) at a higher temperature (300–350°C) in the same way yielded a considerable amount of low-boiling fractionation products with an attendant polymerization, no cycloheptadiene derivative having been detected *at all.* It then appears that in the course of the thermal sigmatropic (3, 3)-rearrangement of divinylcyclopropanes into a 7-membered ring, the reactivity and direction of the thermolysis depend not only on the electronic but also on the steric factors, thus showing in this case too the Woodward-Hoffmann rule to be a selection rule.

In spite of an expected interest in the thermal as well as photochemical isomerizations, to date, there has been no report of studies on thermolysis of oxygen analog of divinylcyclopropane, say, *cis*-2-acetylvinylcyclopropane (**42**).

The present authors have synthesized this compound (**42**) for the purpose of subjecting it to thermolysis. In *a priori* considerations, two ways of rearrangement could be anticipated with this oxygen analog of divinylcyclorpopane on pyrolysis: One would be, as was the case in divinylcyclopropane, a (3,3) sigmatropic rearrangement in which 6 electrons participate in the transition state and therefore is thermally allowed. An alternative possibility would be (2+2) cycloaddition where 4 electrons take part in the concerted mechanism of the transition state and consequently is in usual photochemically favored.



In the later case, there should be two possibilities of reaction, *i.e.* the participation of carbonyl in the concerted mechanism would lead to a cycloether ring (**47**) formation, whereas that of vinyl group to a cyclopentene derivative. The pyrolysis of (**42**) at 160°C afforded 4-acetylcyclopentene (**48**) exclusively. The higher selectivity of this rearrangement was evidenced by the yield of (**48**) up to 80%, as analyzed by vpc. The structure of the thermolysis product (**48**) was fully substantiated by the IR, NMR- and MAS-spectral analyses.

III. EXPERIMENTAL

Ethyl 2-acetoxymethylcyclopropanecarboxylate (17):

Ethyl diazoacetate (13.6 g; 0.014 mole) was added dropwise into allyl acetate (36 g;

0.316 mole) in the presence of anhydrous cupric sulfate (0.2 g) under reflux, and the addition was adjusted so as to ensure smooth evolution of nitrogen gas (93% of the theory). The distillation of the reaction mixture yielded crude ester in a 70% yield. After the treatment of this product with 3% cold permanganate solution, pure sample of ethyl 2-acetoxymethylcyclopropanecarboxylate (**17**) was obtained. bp. 128-9°C/22 mm; n_D^{20} 1.4432. (13.3 g; 60%). IR-spectrum; 1240 cm^{-1} and 1728 cm^{-1} (CO).

2-Hydroxymethylcyclopropanecarboxylic acid (18):

The ester (**17**) (3.7 g; 0.02 mol) was refluxed with aqueous 2N-KOH solution until the mixture became transparent and the careful neutralization and extraction gave *trans*-2-hydroxymethylcyclopropanecarboxylic acid, mp. 64-5°C; Analysis. Found C, 51.72: H, 6.94; Calcd. for $C_5H_8O_3$; C, 51.54: H, 6.91. IR-spectrum; 1700 cm^{-1} (CO). Yield 1.3 g (55.7%). As a byproduct, the *cis*-isomer lactone bp. 66–70°C/2 mm, n_D^{20} 1.4620. was obtained (0.41 g; 21%).

Mehtyl *trans*-2-hydroxymethylcyclopropanecarboxylate (19):

By the standard method with diazomethane, the *trans*-acid (**18**) was converted into the corresponding methyl ester in nearly quantitative yield. bp. 122-5°C/17 mm, n_D^{25} 1.4580. IR-spectrum: 1728 cm^{-1} (ester group), 3500 cm^{-1} (OH).

Methyl *trans*-2-formylcyclopropanecarboxylate (20):

a) With Attenburrow MnO_2.[11] The *trans*-ester (**19**) (5 g; 0.038 mole) was shaken with active manganese dioxide (31 g) in ether at 20°C for 16 hr. After filtration, manganese dioxide was washed with ether and the combined ethereal solution was evaporated, and the distillation of the residue yielded *trans*-2-formylcyclopropanecarboxylate (**20**), bp. 105–110°C/20 mm, n_D^{25} 1.4568. Yield 3.4 g (70%).
IR-spectrum: 1730 cm^{-1} (CO).
b) With silver carbonate[12]: A large excess of silver carbonate (104.7 g; 0.38 mole) was suspended in the benzene solution (60 ml) of the carbinol (**19**) (5 g; 0.038 mole). Some benzene was distilled off azeotropically and then the solution was refluxed for 8 hr. The solid was removed by filtration and the formyl derivative (**20**) was obtained in the usual manner. bp. 106–110°C/20 mm, n_D^{25} 1.4568. Yield 3.7 g (80%).

***n*-Pentyltriphenylphosphonium bromide:**

A mixture of triphenylphosphine (26.2 g; 0.1 mole) and *n*-pentyl bromide (15.5 g; 0.1 mole) in benzene (50 ml) was refluxed with stirring for 24 hr. After the duration, the mixture was allowed to cool and the supernatant liquid was discarded from the viscous oil. The oil was mixed with ether, whereupon the resulting pasty mass solidified after standing at room temperature for several hr. The solid was triturated several times with ether and dried *in vacuo* over phosphorus pentoxide to afford 36.9 g (90%) of a solid melting at 166–8°C. *n*-Pentyltriphenylphosphonium bromide was stored in a capped bottle in a desicator. Anal. Calcd. for $C_{23}H_{26}PBr$: C, 66.83: H, 6.34: Found C, 66.96: H, 6.35.

Methyl *trans*-2-(*trans*-1′-hexenyl)-cyclopropanecarboxylate (21-a):

To a stirred suspension of *n*-pentyltriphenylphosphonium bromide (8.26 g; 0.02 mole)

in dry ether-tetrahydrofuran (30 ml+30 ml) under a nitrogen atmosphere, was added butyl lithium (1.9 g; 0.03 mole) in hexane at −20°C. The resulting deep red solution was cooled to −40°C in a dry-ice-acetone bath and to this was added a solution of the aldehyde (**20**) (2.6 g; 0.02 mole) in dry ether (10 ml)over a period of 5 min. during which the bath temperature was maintained at −30°C. A heavy, cream-colored suspension resulted almost immediately. After one hour's stirring, butyl lithium (1.9 g; 0.03 mole) was added to the reaction mixture and then was added potassium *tert*-butylate (8.5 g; 0.46 mole). The reaction mixture was decomposed with water and the organic layer was separated. The aqueous layer was extracted with ether (150 ml) and the combined extract was dried over anhydrous sodium sulfate. The evaporation and distillation through an effective column of the ethereal solution gave methyl *trans*-2-hexenylcyclorpopane carboxylate, bp. 125−30°C/20 mm. (1.46 g ; 40%), n_D^{19} 1.4670. This product constituted of two isomers as indicated by two peaks in vpc.

A second final work-up procedure was sometimes used whereupon after removal of the solvent from the dried ethereal solution, dry petroleum ether (bp. 30–60°C) was added to the remaining oil until precipitation ceased. The mixture was allowed to stand still for 1 hr., when the supernatant liquid was discarded from the solid material, consisting largely of triphenylphosphine oxide, mp. 148–152°C and most of the petroleum ether was removed. The remaining oil was subsequently fractionated. Comparable yields were obtained by either route.

Qualitative vpc analyses afforded successful separation of the product into two peaks. The area under the first and smaller peak could be augmented proportionally with respect to that under the second peak, or *vice versa* by the use of mixtures of the pure isomers; *trans*-2-(*trans*-1′-hexenyl)-(**21**-a), *trans*-2-(*cis*-1′-hexenyl)-cyclopropane-carboxylates (**21**-a′) respectively. The *cis*-isomer was thus shown to be predominant in this reaction product (*cis* : *trans* 6 : 4). The preponderance of the *cis*-side chain isomer (**21**-a′) was found to vary depending on the reaction conditions. IR-absorption bands were observed for (**21**-b) and (**21**-a′) at 1670, 965 and 600 cm^{-1}. The bands at 965 cm^{-1} was of intermediate strength as compared with the very intense absorption exhibited by the *trans*-isomer (**21**-a) and very weak absorption exhibited by the *cis*-isomer (**21**-a′) in this region. Moreover, the *cis*-isomer, not the *trans*-isomer, showed absorption in the region of 690 cm^{-1}.

b) A solution of butyl lithium (1.9 g; 0.03 mole) was added under nitrogen stream to a suspension of pentyltriphenylphosphonium bromide (8.3 g; 0.02 mole) in absolute ether (30 ml) at 0°C, the mixture first became orange-red and then deep red. After several min., a solution of the aldehyde (**20**) (2.6 g; 0.02 mole) in ether (5 ml) was added, and the mixture stood still at room temperature. A gray-brown precipitate separated, leaving the supernatant solution of orage-yellow color. After 2 hr, the precipitate was filtered, washed with ether and the ethereal solution was washed with water and dried over potassium carbonate. After evaporation of the solvent and removal of triphenylphosphine oxide, the distillation of the residue through an effective column gave the product (**21**-a), bp. 124−30°C/20 mm, n_D^{19} 1.4671. Yield 1.4 g (80%).

***trans*-2-Hydroxymethyl-(*trans*-1′-hexenyl)-cyclopropane (22-a):**

The lithium aluminum hydride (0.4 g; 0.01 mole) reduction in the standard procedure

of the ester (**21**-a) (1.8 g; 0.01 mole) gave the corresponding cyclopropylcarbinol (**22**-a), bp. 115—20°C/20 mm, n_D^{22} 1.4702. Yield 1.4 g (90%).
IR-spectrum: 3410 cm^{-1} (OH), 960 cm^{-1} (*trans*-ethylene).

Oxidation of (**22**-a): a) With active manganese dioxide: By the same procedure as described above (with (**20**)). The carbinol (**22**-a) was oxidized with active MnO_2 to give the corresponding aldehyde, *trans*-2-formyl-(*trans*-1′-hexenyl)-cyclopropane (**23**-a) in an 82% yield. bp. 105—7°C/20 mm, n_D^{25} 1.4702.
b) With silver carbonate: Exactly the same procedure was followed for (**22**-a) and the yield of the oxidation product (**23**-a) was found satisfactory enough (85%).
Methyltriphenylphosphonium bromide: This compound was obtained from methyl bromide and triphenylphosphine by the usual method. mp. 227–229°C. Anal. Calcd. for $C_{19}H_{18}PBr$: C, 63.87; H, 5.079: Found C, 63.87: H, 508.

(±)-Dictyopterene A (8′):

Methyltriphenylphosphonium bromide (3.69 g; 0.01 mole), suspended in dry ether-tetrahydrofuran(20 ml), was treated under nitrogen with *n*-butyl lithium (0.015 mole), the solid rapidly dissolved and the red solution was kept at 0°C for 2 hr. After the addition of the aldehyde (**23**-a) (1.3 g; 0.01 mole) in either, the mixture was kept at 0°C for 2 hr. Removal of solvent and the distillation of the residue afforded (±)-dictyopterene A (**8′**). bp. 72-5°C/18mm, n_D^{20} 1.4682. Yield 1.2 g (80%). The vpc of this product indicated the presence of two isomers as shown by two peaks.

Isolation of (±)-dictyopterene A (8′) by preparative vpc.

The compounds (**8′**) and (**24**) were subjected to preparative vpc separation under the following conditions:

Aerograph	;	A-700, Detector; TCD
Column	:	P. G. S., 120°C
Injector	:	140°C, Collector 150°C
Gas flows	:	150 ml/min.
Retention time	:	20 min. for (**8′**) and 22 min. for (**24**)

Synthesis of dictyopterene A via route B:

Methyltriphenylphosphonium bromide (3.6 g; 0.01 mole) was allowed to react with butyl lithium (0.8 g; 0.015 mole) in absolute ether. The color of the solution was initially deep red and turned orange in 2 hr. The cyclopropanecarboxyaldehyde (**20**) (1.3 g; 0.01 mole) was then added with stirring. The white slurry was stirred for additional 2 hr and filtered; the filtrate was washed with ether, and residue was distilled to give *trans*-2-vinylcyclopropanecarboxylate (**21**-b), bp 44–5°C/15 mm, n_D^{20} 1.4725. Yield 1.1 g (80%).
IR-: 1730 cm^{-1} (CO); 1638 cm^{-1} ($CH=CH_2$).

***trans*-2-Hydroxymethylvinylcyclopropane (22-b):**

The preceding ester (**21**-b) was reduced with lithium aluminum hydride in the usual way to give the carbinol (**22**-b). bp. 45–50°C/15 mm, n_D^{25} 1.4720 (Yield 97%).
IR: 3350 cm^{-1} (OH), 1640 cm^{-1} ($CH=CH_2$).

***trans*-2-Formylvinylcyclopropane (23-b):**

This compound was prepared by the same procedure as with (**20**), using active manganese dioxide or silver carbonate. bp. 43–5°C/15 mm, n_D^{25} 1.4705. Yield 80%.

(±)-Dictyopterene A (8′):

Following the usual procedure of the Wittig synthesis, the reaction of vinylcyclopropanecarboxyaldehyde (**23**-b) with the ylid from pentyltriphenylphosphonium bromide and butyl lithium yielded (±)-dictyopterene A, *trans*-2-vinyl-(*trans*-1′-hexenyl)-cyclopropane (**8′**), in an 82% yield. bp. 74–5°C/18 mm, n_D^{20} 1.4670.

The IR-, NMR- and MAS-spectra of this synthetic racemic specimen were identical in every respect with those of naturally derived (+)-dictyopterene A (**8**), which were supplied by Dr. Moore.[5]

IR: 3080 cm^{-1}, 1640 cm^{-1} (vinyl group), 2990 cm^{-1}, 1030 cm^{-1} and 848 cm^{-1} (cyclopropane); 958 cm^{-1}, 1665 cm^{-1} (*trans*-disubstituted double bond).

MAS: 150 (5.8): m/e; 135(0.1), 121(3.1), 109(2.1), 108(4.7), 107(7.5), 105(3.4), 94(13), 93(37), 91(29), 80(41), 79(100), 78(14.3), 77(26.5), 67(18), 55(11), 41(31.5), 39(17.3).

(±)-*cis*-Chrysanthemol (30):

cis-Chrysanthemic acid (**28**) (4 g; 0.024 mole) in absolute ether (40 ml) cooled in ice–water was reduced by the addition of lithium aluminium hydride (1.8 g; 0.04 mole) under effective stirring. The temperature was raised gradually to room temperature and was stirred for additional 2 hr. The reaction mixture was decomposed with ice–cold 2N-hydrochloric acid solution by cooling externally. The fractionation of the combined ethereal extract gave *cis*-chrysanthemol (**30**). bp. 80–1°C/5 mm, n_D^{20} 1.4748 (lit. bp. 80°C/5 mm). Yield 3.52 g (95%). This compound was obtained also from the corresponding ester in comparable yields.

(±)-*trans*-Chrysanthemol (27):

The same procedure as illustrated above was followed for *trans*-chrysanthemic acid (**25**) or the ester (**26**) to give the *trans*-carbinol (**27**) bp. 103–8°C/17 mm, n_D^{22} 1.4724 (lit. bp. 105°C/17 mm) in a satisfactory yield (90%).

IR: 3400 cm^{-1} (OH), 1665 cm^{-1} ($\begin{matrix} R \\ R \end{matrix}\!\!>\!\!=\!\!<\!\!\begin{matrix} H \\ \end{matrix}$).

(±)-*cis*-Chrysanthemal (32):

cis-Chrysanthemol (**30**) (1.0 g; 0.006 mole) in petroleum ether (100 ml) was shaken with active MnO_2 (20 g) at room temperature for 24 hr. The reaction mixture was worked up in usual way to give *cis*-chrysanthemal (**32**), bp. 60°C/0.5 mm, n_D^{26} 1.4760 in a 70% yield.

With the use of silver carbonate, the same product (**32**) was obtained in better yield (80%).

(±)-*trans*-Chrysanthemal (31): The *trans*-aldehyde (**31**) was obtained by the same procedure with either MnO_2 or silver carbonate. bp. 65–6°C/2 mm, n_D^{20} 1.4762. Yield 75%.

IR: 1700 cm^{-1} (CO).

General procedure for the synthesis of dictyopterene A analogs.

The Wittig vinylogation of isomeric chrysanthemals (**31**) and (**32**) was exemplified by a typical run of (**31**) with *n*-pentylidenetriphenylphosphorane to lead to *cis*-3,3-dimethyl-2-(*trans*-1′-hexenyl)-(1′-isobutenyl)-cyclopropane (**36**). Essentially the same procedure was followed for other dictyopterene A analogs from isomeric chrysanthemals with the variation of the alkylidenephosphoranes employed.

To a suspension of *n*-pentyltriphenylphosphonium bromide in dry ether-THF (20 ml) was added *n*-butyl lithium (0.9 g; 0.015 mole) under nitrogen at 0°C. The solution became initially orange-red and then turned deep red in 2 hr. After stirring for 1 hr a solution of the aldehyde (**32**) (1.5 g; 0.01 mole) in ether (10 ml) was added dropwise. When the reaction completed, the precipitate was filtered, washed with ether and the ethereal solution was evaporated and the oil was distilled through an effective column to give, the hydrocaron (**36**) bp. 113–5°C/20 mm, n_D^{25} 1.4682. Yeild 88%.

IR: 1640 cm^{-1} (C=C), 960 cm^{-1} (*trans*-ethylene).
NMR; 1.15 ppm (3H, CH_3-◁), 0.99 ppm (3H, CH_3-◁) 1.703, 1.68 ppm (6H, d, J 1.5 cps, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!=\!<$), 5.0 ppm (1H, dm, $>\!=\!<^{H}$), 2.08 ppm (2H, q. J 7 cps, $-CH_2-CH_2-CH=$), 5.30 ppm (2H, $_{H}\!>\!=\!<^{H}$); 0.9–1.6 ppm (9H).

trans-3,3-Dimethyl-2-(*trans*-1′-hexenyl)-(1′-*iso*butenyl)-cyclopropane (**34**). bp. 114–6°C/20 mm, n_D^{25} 1.4670.
IR: 1640 cm^{-1} (C=C), 960 cm^{-1} (trans-ethylene).
NMR: 1.12 ppm (6H, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>$◁), 1.70 ppm (6H, s, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!=\!<$) 4.95 ppm (1H, dm, $=\!<^{H}$) 2.31 ppm (2H, q, J 7 cps $-CH_2-CH_2-CH=$) 5.30 ppm (2H, $^{H}\!>\!=\!<_{H}$), 0.9–1.6 ppm (9H).

cis-3,3-Dimethyl-2-(1′-*iso*butenyl)vinylcyclopropane (**35**). 66–8°C/17 mm, n_D^{20} 1.4622. IR: 3080, 1790, 1633, 987, 890 cm^{-1} ($-CH=CH_2$)
NMR: 1.13 ppm (3H, CH_3-◁), 1.05 ppm (3H, ▷-CH_3), 1.77, 1.71 ppm (6H, d, J∼1, 5 cps $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>$C=C-), 5.37 ppm (1H, dm, J∼8), 4.94, 5.36 ppm (3H, $^{H}\!>\!=\!<^{H}_{H}$) 1.2, 1.60 ppm (2H, $^{H}\!\!\diagdown\!\!\triangledown\!\!\diagup^{H}$).

trans-3,3-Dimethyl-2-(1′-*iso*butenyl)-vinylcyclopropane (**33**). 68–9°C/17 mm, n_D^{20} 1.4632.
IR-Spectrum: 3080, 1790, 1633, 987, 890 cm^{-1} ($-CH=CH_2$).
NMR: 1.12 ppm (3H, ▷$<^{CH_3}$), 1.04 ppm (3H, ▽$\diagdown CH_3$), 1.70 ppm (6H, S, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!=\!<$), 4.81 ppm 1H, J∼8, $>\!=\!<^{H}$), 4.98, 5.0 ppm (3H, $^{H}\!>\!=\!<^{H}_{H}$), 1.38 ppm (2H, $H\diagup\!\!\triangledown\!\!\diagup^{H}$).

4-Chloro-2-*cis*-butene-1-ol (38):

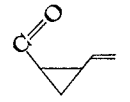
A mixture of *cis*-2-butene-1,4-diol (**37**) (50 g: 0.568 mole) and pyridine (38 ml) in dry

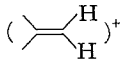
ether (95 ml) was cooled to −5°C. Thionyl chloride (4 ml, 0.34 mole) was added to the solution maintaining the reaction temperature at −5°C to 2°C. After stirring for 2 hr, the resulting mixture was poured into ice-water, extracted with ether and dried. The distillation of the ethereal extract gave 4-chloro-*cis*-2-butene-1-ol (**38**), bp 79–81°C/11mm, n_D^{25} 1.4837. Yield 28.3 g (47%).
IR:3400 cm^{-1} (OH).

***cis*-2-Acetylvinylcyclopropane (42).**

The condensation of 4-chloro-*cis*-2-butene-1-ol (**38**) (15 g; 0.141 mole) with ethyl acetoacetate (**39**) (12 g: 0.1 mole) in the presence of sodium ethylate (2.6 g) in ethanol (50 ml) gave, after the usual work-up of the reaction mixture, a crude ketone, 1-hydroxy-hept-2-ene-6-one (**41**). The distillation of the crude ketone (**41**) from acidic ethereal solution yielded *cis*-2-acetyl-vinyl-cyclopropane (**42**). bp. 51–5°C/5 mm, in an 85% yield.
In an alternative way, the crude hydroxyketone (**41**) was heated with phosphoric acid to give the same acetylvinyl-cyclopropane (**42**) in a 40% yield. This procedure was accompanied by considerable polymerization.

IR: 1690 cm^{-1} (C=O), 3070, 1640, 910 cm^{-1} ($CH=CH_2$)
NMR: 2.28 ppm (3H, s, CH_3-), 2.1∼1.0 ppm (4H), 5∼5.7 ppm (3H)

MAS: 110 m/e (M^+), 95 m/e  , 43 m/e , 67 m/e

 , 27m/e 

Pyrolysis experiments:

Heating of (**8′**) at 175°C for 3 hr gave the rearrangement product, 3,6-*n*-butyl-cyclohepta-1.4-diene (**46**). After purification by preparative vpc, the product (**46**) showed the following physical properties in agreement with the description in literature.[8]

IR-spectrum : 3030 cm^{-1}, 1650 cm^{-1} (double bond),
NMR-spectrum: 0.90 ppm (3H, t, J 5 cps, CH_3)
1.30 ppm (6H, m, $-CH_2-CH_2-CH_2-$)
2.15 ppm (2H, m, $-CH=CH-CH_2CH=$)
2.75 ppm (2H, m, $-CH=CH\cdot CH_2CH=CH$)
5.55 ppm (4H, m, $-CH=CH\cdot CH_2CH=CH$)
2.32 ppm (1H, m, $-CH=CH-CH\langle^{CH_2}_{CH_2}\rangle$)

Pyrolysis was conducted in a sealed tube under deduced pressure at/or below 0.1 mm Hg at appropriate temperatures.

Pyrolysis of *cis*-3,3-dimethyl-2-vinyl-*iso*butenyl-cyclopropane (35):

In a preliminary experiment, the sample (**35**) was heated at 200–250°C, and recovered unchanged. When treated at 300–350°C, it decomposed to yield a considerable amount of low-boiling compounds and partially polymerized, as being checked by means of vpc.

The compound (**42**) was heated at 160°C to yield 4-acetyl-cyclopentene (**48**) after 15 hr, according to vpc analysis. Preparative vpc separation (on a column of PGS on Aerograph instrument) provided pure samples of this product (**48**).

The resulting product gave the IR-, NMR- and MAS-spectra to be expected for such a structure.

IR : 1700 cm^{-1} (-C=O), 1660 cm^{-1} (-C=C-), 760, 695 cm^{-1}  .

NMR : 2.25 ppm (3H, s, $-CO-CH_3$),

5.78 ppm (2H, t, J 2.2 cps, )

: 2.40 ppm ~ 2.80 ppm (6H).

MAS : 110 m/e (M^+), 95 m/e ()$^+$, 67 m/e ()$^+$, 43 m/e $(CH_3-\overset{O}{\overset{\|}{C}}-)^+$.

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