POLYCYCLIC DITERPENOIDS BIOGENETICALLY RELATED TO THE CEMBRANOIDS

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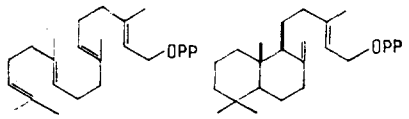
This review describes cyclocembrane compounds isolated from plants, marine organisms, and insects. A systematization of cyclized diterpenoids according to the types of carbon skeletons is given.

A group of substances known under the general name diterpenoids is widely distributed in the plant and animal world. The systematization of their structure is based primarily on biogenetic ideas. The common biogenetic precursor of all diterpeniods is considered to be geranylgeranyl pyrophosphate (1), the enzymatic cyclization of which leads to the successive formation of all the multiplicity of bi-, tri-, tetra-, and pentacyclic diterpenoids [1]. Most of these compounds have labddienyl pyrophosphate (2) or its antipode as their bicyclic precursor. Among other groups of diterpenoids, the formation of the carbon skeletons of which takes place by a different pathway of the cyclization of geranylgeranyl pyrophosphate cembranoids-diterpenoids with the macrocyclic fourteen-carbon ring of 1-isopropyl-4,8,12-trimethylcyclotetradecane (3) — have been particularly singled out in the last two decades.



(1) (2)

Since the time when the structure of cembrene — the first known cembranoid [2, 3] — was established, numerous publications devoted to the isolation of compounds of this type from various natural sources have appeared. Weinheimer generalized these publications in his review [4].

The hypothesis that cembranoids may be precursors of other polycyclic diterpenoids was first put forward in 1964 by Erdtman [5]. Since this time, bi-, tri-, and tetracyclic diterpenoids the structures of which are logically deduced from the cembrane carbon skeleton by successive cyclizations have been found in plants and marine organisms and even in insects. These compounds not infrequently possess a high biological activity which explains, in particular, the ever-increasing interest in them on the part of the workers of various countries. In the present review, an attempt is made for the first time to generalize information on polycyclic diterpenoids of this type from the point of view of their presumed biogenetic relationship. The formal bond of the basic structural types of the cyclocembranoids is shown in the scheme (see following page).*

The names of the types have been given from the names of the first known representatives with such carbon skeletons. It is interesting to note that the diterpenoids corresponding to them, apart from the eunicillane compounds, are produced, most probably, as the result of the electrophilic cyclization of the most common cembranoid — neocembrene (12) — followed by oxidation. This hydrocarbon is found in conifers [6, 7] of the Pinaceae family, plants of other species [8], corals [9], and termites [10]. In actual fact, the protonation of its molecule at one of the positions C_7, C_{11}, or C_{16} with the subsequent participation of the C_3, C_{15}, or C_{11} double bond should lead to briareane, secotrinervitane, and verticillane derivatives, respectively (see following page).

*We introduce the term "cyclocembranoids" for convenience of denoting compounds formed by the transannular cyclization within the 14-membered macrocyclic system of cembrane.

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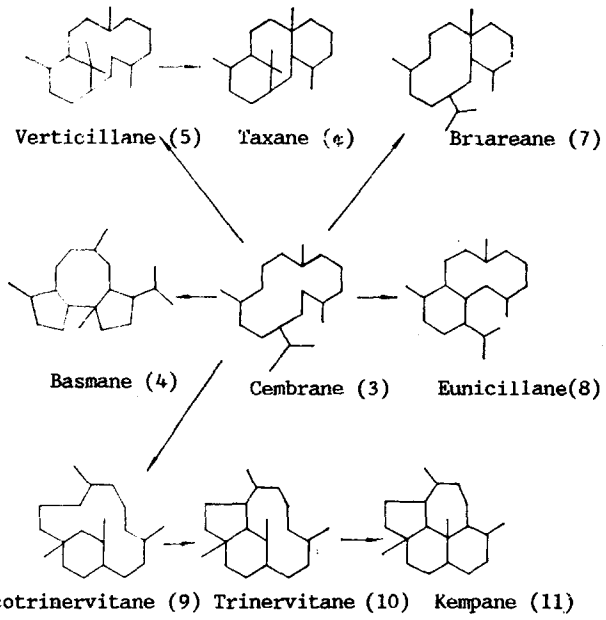
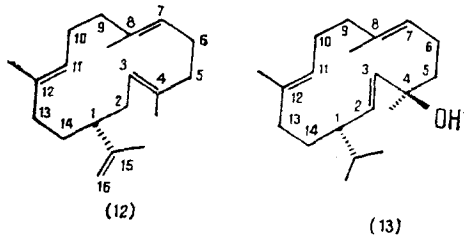




(12) (13)

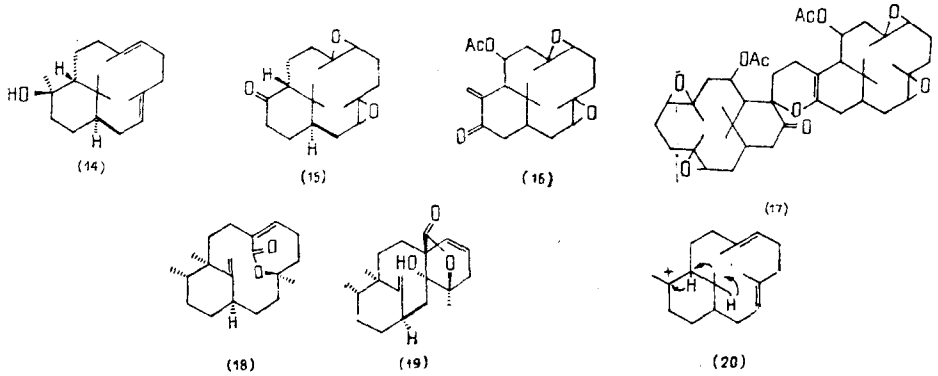
Theoretically, eunicillane derivatives can be formed as the result of the splitting out of a ^{-}OH anion from the isocembrol molecule (13) with the subsequent involvement of the C_{11} double bond. Isocembrol itself is a well-known component of plants [7] and soft corals [11].

Cyclocembranoids of certain types are formed in various living organisms in the process of biosynthesis. Thus, verticillane and taxane derivatives have been found only in plants, eunicillane and briareane diterpenoids only in marine organisms, while secotrinervitanes and the products of their further cyclizations have been detected in termites. This is most probably connected with features of the enzymatic systems leading to the metabolism of the cembranoids in the corresponding organisms.

CYCLOCEMBRANOIDS OF PLANTS

Verticillane Diterpenoids

The first known bicyclocembranoid was verticillol (14), isolated by Erdtman [5] from the heartwood of *Sciadopitus verticillata* Sieb, et Zucc. The structure of verticillol was shown by a x-ray structural analysis of its diepoxide and its absolute configuration by an investigation of the circular dichroism of the diepoxyketone (15) obtained from it [12]. Later, verticillol was found by Hasegawa [13] in the seeds of the same plant.



(14) (15) (16) (17) (18) (19) (20)

A more complex derivative of verticillane — hypoestoxide (16) — was isolated by Adesomoju [14] from a hexane extract of the epigeal part of the plant *Hypoestes rosea* (family Acanthaceae) Its structure was established by x-ray structural analysis. In a further consideration of the composition of an extract of the same plant, Adesomoju [15] isolated a bisverticillane derivative — dihypoestoxide (17). From the formal point of view, it is a product of the Diels-Alder reaction of two molecules of hypoestoxide.

It is interesting to note that the verticillane diterpenoids known in plants at the present time are not accompanied by cembrane derivatives, which may show either a rapid metabolism of the intermediate cembranoids or that the latter are not formed during the biosynthesis of the verticillanes as intermediate compounds.

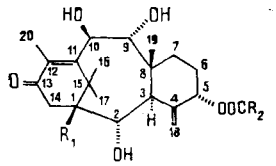
The range of diterpenoids known at the present time is limited to the three verticillanoids considered above. A compound with a modified verticillane carbon skeleton — cleomeolide (18) — was isolated by Burke (16) from a benzene extract of the leaves of the plant *Cleome viscosa* L. (Capparaceae) growing in Jamaica. Its structure was established by x-ray structural analysis.

On oxidation by the Jones a reagent in acetone, cleomeolide (18) gives the corresponding ketone which is converted a 10% metanolic solution of potassium hydroxide by intramolecular isomerization with the formation of the hydroxy lactone (19) with a modified taxane carbon skeleton. Burke [16] suggests that the carbon skeleton of cleomeolide is formed via the cation (20) obtained, in its turn, from a cembrane precursor.

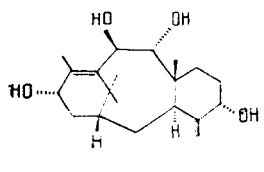
Taxane Diterpenoids

Diterpenoids with the carbon skeleton of taxane (6) have so far been found only in species of yew (*Taxus* L., Taxaceae), two widely distributed species having been subjected to the most detailed study — English yew (*Tuxus baccata* L.) and Japanese yew (*Taxus cuspidata* Pilg. et Zucc.). The name "taxane" has been adopted in the official nomenclature of the diterpenoids [17]. It must be mentioned that the numbering of the carbon atoms in it differs from that proposed initially [18].

In the historical respect, the taxanoids are some of the longest-known. As early as 1856, Lukas [19] isolated the poisonous principle from the leaves of English yew, which he called taxin and which possessed the properties of an alkaloid. In 1956, Graf [20] established the nature of the hydrogen-containing residue of its molecule obtained on the acid hydrolysis of taxin as β-(dimethylamino)hydrocinnamic acid. This moiety of the taxin molecule is extremely labile and under the action on taxin of potassium carbonate in aqueous solution is converted into a cinnamic acid residue with the elimination of dimethylamine. The nitrogen-free product so obtained is, as established by Baxter [21, 22], not an individual compound but a mixture of substances the main one of which was isolated and called O-cinnamoyltaxicin-I, while one of the minor ones was called O-cinnamoyltaxicin-II. The structures of these diterpenoids required painstaking work and were established simultaneously by three groups of chemists [23-25] who, in a following combined publication [26] suggested the name "taxane" for the hydrocarbon skeleton of the diterpenoid moiety of the taxcin molecules. The structures of taxicin I, taxicin II and O-cinnamoyltaxicins-I and -II are expressed by formulas (21)-(24), respectively. The triacetate of O-cinnamoyltaxicin-II was originally described by Japanese chemists under the name of "taxinin" [24, 25]. It was found in the leaves of the Japanese yew [25].



(21) R_1 = OH, R_2 = $CH_2CH(NMe_2)Ph$
(22) R_1 = H , R_2 = $CH_2CH(NMe_2)Ph$
(23) R_1 = OH, R_2 = CH = CHPh
(24) R_1 = H , R_2 = CH = CHPh



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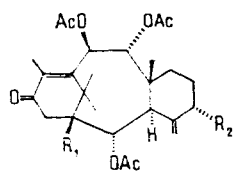
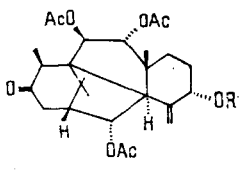


(26) R_1 = OH, R_2 = OH
(27) R_1 = H , R_2 = OAc



(28) R = H
(29) R = Ac

The stereochemistry of the diterpenoid moiety of taxicins-I and -II was elucidated in 1965 by Dukes [27]. Another variant of the stereochemistry, which however, proved to be incorrect, was given in a paper by Nakananishi [28]. The correctness of Dukes' conclusions was confirmed after a year by the results of x-ray structural analysis [29]. The completion of the work on establishing the structure and stereochemistry of the taxicins [20] gave an impulse to work on the search for new taxanoids and facilitated the task of determining their structures, although authors were frequently forced to turn to x-ray structural analysis.

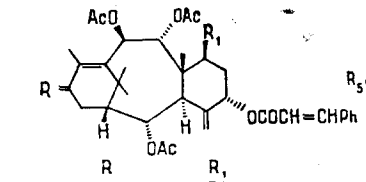
From the hartwood of the English yew, Chan [31] isolated the simplest of known taxanoids — the tetraol (25) — while its tetraacetate (taxusin) was found in the heartwood of the Japanese yew [32].

In a detailed investigation of the taxanoids of the leaves of the Japanese yew, Chiang [33] isolated from them, in addition to taxinin, O-cinnamoyltaxicin-I triacetate and the new compounds taxinins A, H, K, and L having structures expressed by formulas (26)-(29), respectively.

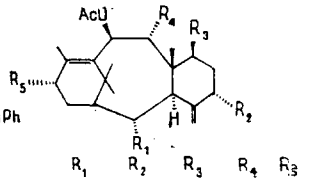
In a further study of this material [34], the authors isolated, in addition, taxinins B (30), E (31), and J (32). To establish the structures and stereochemistries of the substances obtained successful use was made of observations of the intramolecular Overhauser effect.

Taxinins K and L, having a 3,11-cyclotaxane carbon skeleton are, apparently, products of the intramolecular photochemical cyclization taking place in the living plant [34]. In a special experiment, the authors showed that when a solution of taxinin A was irradiated with the light of a high-pressure mercury lamp it was converted to the extent of 50% into taxinin K.

In a detailed investigation of the components of the heartwood of the English yew, Mercano [35] isolated, in addition to taxusin [the tetraacetate of the tetraol (25)] seven new taxanoids, five of which had, unlike those described previously, an acetoxy group at C_7. The structures of these compounds are expressed by formulas (33)-(39).

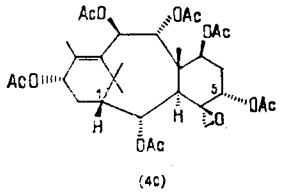


	R	R_1
(30)	=O	OAc
(31)	H, OAc	H
(32)	H, OAc	OAc



	R_1	R_2	R_3	R_4	R_5
(33)	H	OH	H	Ac	OH
(34)	OAc	OAc	H	OAc	OAc
(35)	H	OAc	OAc	OAc	OAc
(36)	OAc	OAc	OAc	OAc	OAc
(37)	*	OAc	OAc	H	H
(38)	*	OH	OAc	OAc	H
(39)	*	OAc	OAc	OAc	H

* – OOCCH(CH$_3$)CH$_2$CH$_3$



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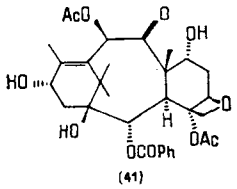

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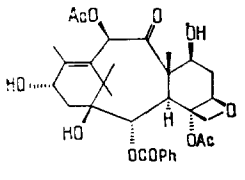

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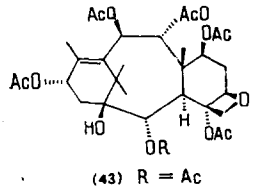
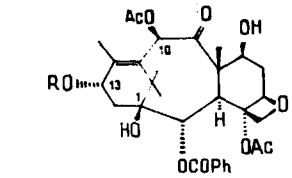


(43) R = Ac
(44) R = COPh
(45) R = CO(CH$_2$)$_4$CH$_3$

In the same source, Marcano found a series of other taxanoids each having an oxygen-containing functional group at C_4 of its molecule: baccatin-I (40), 5-deacetylbaccatin-I

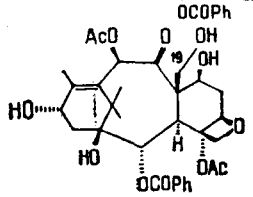
and 1β-hydroxybaccatin-I [36], baccatin-V (41) [37], baccatins-III (42), -IV (43), -VI (44), and -VII (45) and 1-deoxybaccatin-IV [38].

The structures of baccatins-I and -V were established by x-ray structural analysis, and those of the other compounds on the basis of the results of PMR spectra and of chemical transformations. A feature of the molecules of compounds (41)-(45) is the presence of an exetane ring in them. The same ring is present in the molecule of taxol (46), isolated by Wani [39] from the bark of *Taxus brevifolia* and that of cephalomannine (47) — a component of the leaves, stems, and roots of the *Taxus wallishiana* Zucc. [40]. In the plant, the latter accompanies baccatin-III (42) and taxol (46). Cephalomannine and taxol possess a pronounced antitumoral and antileukemic activity [39, 40]. In this connection, the first of them is the subject of a patent [41].



(46) R = OCCH(OH)CH(Ph)NHCOPh

(47) R = OCCH(OH)CH(Ph)NHCOC(Me)=CHMe



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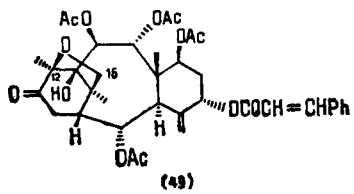

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Wani [39] established that the biological activity of taxol is connected to the presence of an ester group at C_{13}, since the corresponding deacyl derivative (baccatin-III) possesses only 0.001% of the activity of taxol.

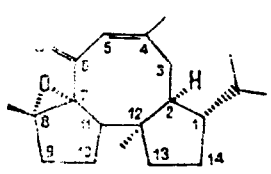
The detection of antitumoral activity in two taxanoids stimulated a further search for similar compounds, and McLaughlin [43] soon discovered in *Taxus wallishiana* another three new taxanoids with similar activity — 19-hydroxybaccatin (48), 10-deacyltaxol, and 10-deacylcephalomannine the structures of which were established on the basis of PMR and mass spectra.

In the molecule of 19-hydroxybaccatin-III, one of the hydroxy groups occupies the C_{19} position, which is unusual for the taxanoids. Another taxanoid with a new position of the functionalization of the taxane carbon skeleton — taxagifin (49) — was isolated in a reinvestigation of an extract of Japanese yew leaves [43]. Its structure was established by x-ray structural analysis.

In view of the detection of an interesting biological activity in taxane diterpenoids in recent years a development of the study of their synthesis has been observed. So far it is possible only to report that some advances have been achieved in the approach to the construction of the carbon skeleton of taxane [44-46]. Attempts to obtain taxane derivatives by cyclizing compounds with the carbon skeleton of verticillane have so far proved unsuccessful [47].

Diterpenoids Basmane

The only known representative of this group — (1S,2S,4Z,7R,8S,11R,12R)-7,8-epoxybasm-4-en-6-one (50) — was isolated by Enzell [48] from an extract of Greek tobacco leaves. Its structure was established by x-ray structural analysis. Since, as can be seen from formula (50), this epoxyketone can



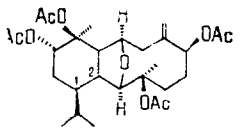
(50)

be obtained formally by the cyclization of a cembrane precursor with the formation of new carbon–carbon bonds between the C_2 and C_{12} and the C_7 and C_{11} atoms, Enzell assumes that it is precisely in this way that it is formed in the plant. Its simpler (bicyclic) precursors are still unknown.

CYCLOCEMBRANOIDS OF MARINE ORGANISMS

Eunicillane Diterpenoids

Representatives fo the still small group of eunicillane diterpenoids have been found in corals of the genera *Eunicella, Muricella* (order Gorgonacea) and *Cladiella* (order Alcyonacea). The first of them — eunicillin (51) — was described by Kennard [49] in 1968 as a component of a petroleum ether extract of the coral *Eunicella stricta*. The structure and the absolute configuration of this diterpenoid was determined by the x-ray structural analysis of its dibromide (the product of the addition of two bromine atoms to the exomethylene double bond). It is interesting to note that the configuration of the isopropyl group in the eunicillin molecule is opposite to that which exists in cembranoids from plants [6, 8] and in corals [50] of the order Alcyonacea.



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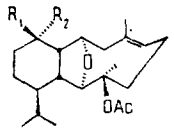
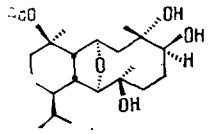


(52) $R_1 + R_2 = CH_2$

(53) $R_1 = OAc$, $R_2 = CH_3$



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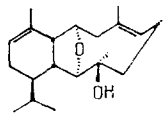

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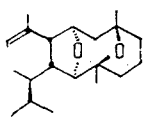

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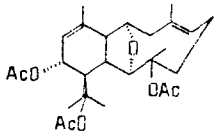

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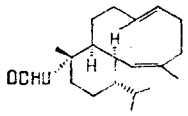

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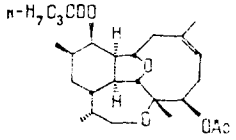

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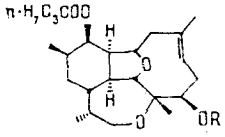
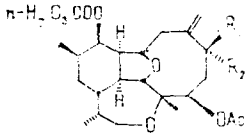


(59) R = Ac

(61) R = H



(62) $R_1 + R_2 = O$

(63) $R_1 = H$, $R_2 = OH$

In this connection, it may be assumed that its biogenetic precursor is a cembranoid compound stereochemically analogous to (+)-S-neocembrene [for example, the antipode of isocembrol (13)]. Such cembranoids are known as components of soft corals of other species [51], although they have not yet been found in *Eunicella* species.

The following two diterpenoids with the same carbon skeleton — cladiellin (52) and acetoxycladiellin (53) — were isolated by Kazlauskas [52] from a soft coral *Cladiella* sp. The structure of compound (53) was shown by x-ray structural analysis, and that of cladiellin by two-stage conversion into the tetraol (54), also obtained from acetoxycladiellin. The absolute configuration of these compounds remains undetermined.

The simplest of the known eunicellanoids — the oxidoalcohol (55) — was isolated by Faulkner [53] from an unidentified species of soft coral. Its structure was proposed on the basis of the results of a detailed analysis of the PMR and ^{13}C NMR spectra and was confirmed by chemical correlation with cladiellin (52). On treatment with boron trifluoride etherate in ether at 0°C, the oxidoalcohol (55) gave the dioxide (56), the catalytic hydrogenation of which led to two epimeric dihydro derivatives. The same two compounds were obtained on the analogous treatment of deacetylcladiellin.

From a *Muricella* coral, Kashman [54] isolated the eunicillanoid ophyrin (57), the structure of which was based on the results of mass, PMR, and ^{13}C NMR spectra and was confirmed by x-ray structural analysis.

A feature of all known eunicillanoids is the cis-linkage of the rings in their molecules. The simplest compound of this type — the formate (58) — was obtained by the action of formic acid on cembrene (4) [55]. This transformation is so far the only example of the biomimetic synthesis of a eunicillin derivative from a cembranoid that has been described.

A series of diterpenoids biogenetically related to the eunicillin diterpenoids has been isolated by Clardy [56] from a methanolic extract of the Caribbean coral *Briareum asbestinum* (order Gorgonacea).

These compounds, which have been called asbestinins-1, -2, -3, -4, and -5 have the structures expressed by formulas (59)-(63). The structure of asbestinin-1 was established on the basis of the results of the x-ray structural analysis of the corresponding dideacyl derivative (diol) and a consideration of the spectral characteristics of products obtained after the performance of the oxidative cleavage of its molecule at the double bond.

The structures of the other asbestinins were shown on the basis of spectral results and a chemical correlation with asbestinin-1. In a further investigation of the composition of this coral, Clardy [57] also isolated asbestinin-2 epoxide and asbestinin-5 6-O-acetate.

The biogenesis of the asbestinins, as is assumed [57], consists in one of the stages of the migration of a methyl group in the molecule of a eunicillane precursor to the neighboring position with the formation of a metabolite with an "asbestinane" carbon skeleton. It must be mentioned that the absolute configurations of the molecules of all the asbestin and eunicillane diterpenoids (apart from eunicillin) have not so far been determined.

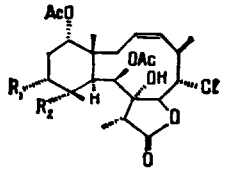
Briareane Diterpenoides

The diterpenoids of this series are represented by highly oxidized metabolites of a number of marine organisms. The first of them to be described was briarein A (64) [58], the structure and absolute configuration of which were determined by x-ray structural analysis. It was isolated from the corals *Briareum asbestinum*.

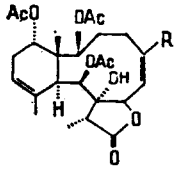
A compound related to this — stylatulide (65) — was detected in *Stylatula* marine polyps [59]. This structure was also determined with the aid of x-ray structural analysis. In a more detailed investigation of an extract of these polyps, Wratten [60] isolated 17-epastylatulide and three new metabolites containing no chlorine atom or conjugated dienic systems in their molecules. Their structures are expressed by formulas (66)-(68). It is assumed that the biological function of compounds similar to briarein A consists in the protection of the marine organisms from mobile predators [60]. Stylatulide is toxic for warm-blooded animals — the LD_{50} value for mice is of the order of 50 mg/kg [59].

Another chlorine-containing diterpenoid — ptilosarcone (69) — has been found in an extract of the sea pen (*Ptilosarcus gurneyi*) [61]. Its structure was established on the basis of the results of an analysis of its PMR spectromy.

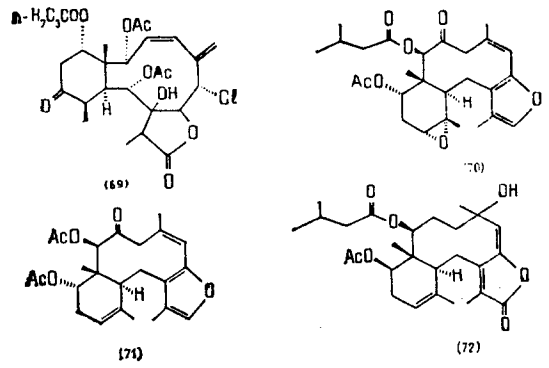
From another species of sea pen (*Scytalium tentaculatum*), Australian chemists [62] have isolated a series of new briareane diterpenoids for which structures (70)-(72) have been proposed on the basis of spectral characteristics.



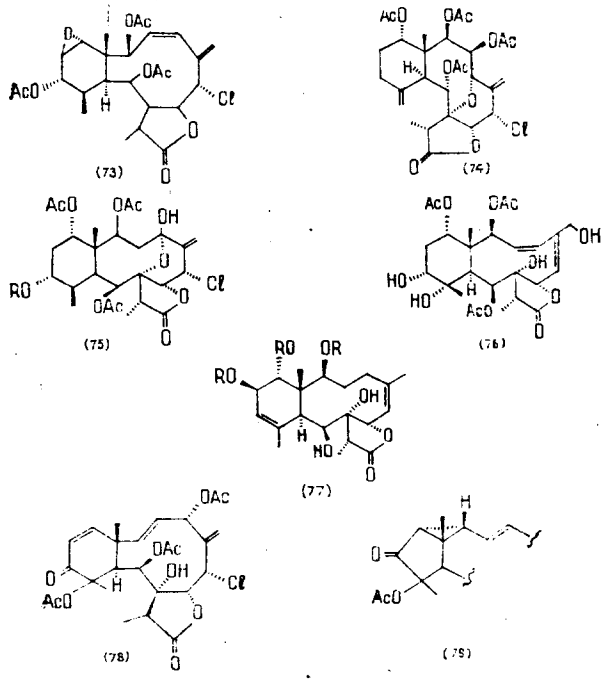
(64) $R_1=R_2=OAc$
(65) $R_1+R_2=O$



(66) R = Me
(67) R = CH_2CH
(68) R = $COCCH_3$



Another two briareane diterpenoids — brianthein (73) and junceellin (74) — have been isolated from the coral *Briareum polyanthes* [63] and the medusa *Junicella squamata* [64], respectively. The structure of the first of them was established by comparing its spectral characteristics with those of briarin A, and that of the second by x-ray structural analysis.



A series of new briareane diterpenoids has been described by French chemists who investigated two species of C_{10} from the New Caledonia region. From *Pteroides laboutei* they isolated pteroidin (75), 12-O-benzoyl-12-O-diacetyl pteroidin and laboutein (76) [65], and from *Cavernulina grandiflora* three compounds with the general formula (77), where R = acetyl, propionyl, or n-butyryl [66]. Their structures were proposed on the basis of spectral characteristics, and the precise positions of the acyl residues in the molecules are still unknown.

The chlorine-containing briaranoid erythrolide B (78) has been detected in the Caribbean coral *Erythropodium caribaeorum* together with a diterpenoid having a new carbon skeleton — erythrolide A (79), which is the product of the phototransformation of the former [67]. The conversion of (79) into (78) takes place both on irradiation with the light of a mercury lamp and also under conditions imitating natural conditions — in the sunlight in a 5% methanolic solution of seawater. In the latter case, the degree of conversion of compound (78) after eight days was 37%.

The great diversity of the structures of the briareane derivatives known at the present time when their wide distribution permit the assumption that in future such compounds will form a fairly numerous group of natural cyclocembranoids.

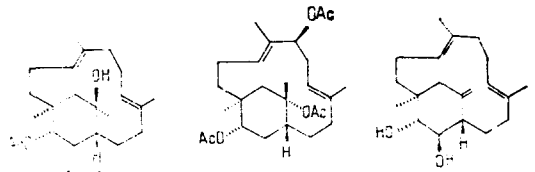
TERMITE CYCLOCEMBRANOIDS

The establishment of the diterpene nature of the trail pheromone of termites and its identification as a neocembrene ("neocembrene A") [10, 6] stimulated further work on the in-

vestigation of the terpenoid components of extracts from these insects. It was found that the protective secretion of all the species of soldier termites investigated contained diterpenoids with original carbon skeletons not found among the metabolites of plants and marine organisms. Investigations on the isolation and determination of the structures of these compounds have developed mainly since 1976 when a paper by Prestwich [68] was published on the determination of the structure of a diterpenoid with a trinervitane carbon skeleton. Compounds with bi- and tetracyclic skeletons related to the trinervitanes were described subsequently.

7,16-Secotrinervitane Diterpenoids

So far there are few compounds of this series. The hydroxyacetate (80) was isolated by Braekman [69] from *Nasutitermes princeps*, and the triacetate (81) by Baker [70] from *Constrictotermes cyphergaster*. The structures of those compounds were established with the aid of x-ray structural analysis but their absolute configurations so far remain unknown.

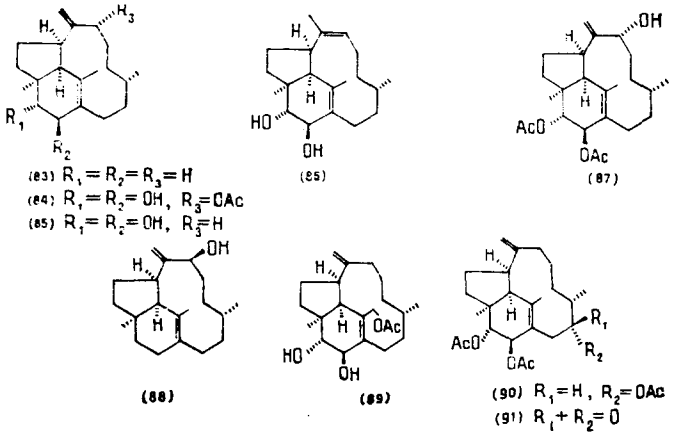


(80) (81) (82)

The diol (82) is known as a component of the termites *Longipeditermes longipes* [71].

Trinervitane Diterpenoids

Derivatives of the so far unknown hydrocarbon trinervitadiene (83) are the most numerous among the termite metabolites known at the present time. The first compound of this series — the acetate (84) — was isolated by Prestwich [68] from an extract or the heads of the soldier termites Trinervitermes gratiosus . Its structure was established by x-ray structural analysis and its absolute configuration from the sign of the Cotton effect on the circular dichroism curve for the chelate with praseodymium trisdipivaloylmethanante.

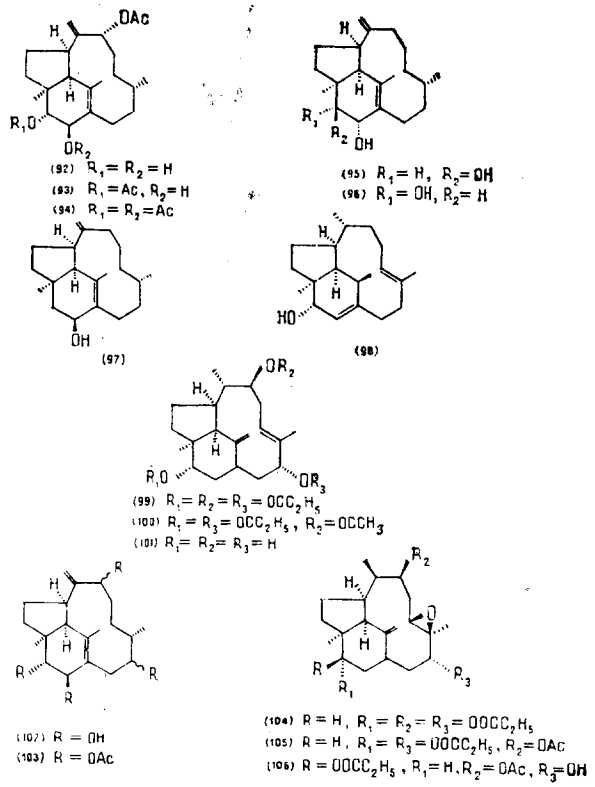


Subsequently, Prestwich [72] isolated from the same species of termites another three new compounds with structures (85), (86), and (87), and from *Trinervitermes bettonainus* (85), (88), and (89), the structures of which were deduced on the basis of spectral characteristics, mainly the results of an analysis of PMR spectra. He found that these diterpenoids [apart from (87) and (89)] were also present in other species of termites of the genus *Trinervitermes*.

In an investigation of the composition of an extract from the Cuban termites *Nasutitermes rippertii*, Vrkoc found various trinervitane the derivatives (88) and (90)-(94) in it, and in the species *Nasutitermes costalis* he detected two diols (95) and (96), a feature of which is the α-configuration of the hydroxy group at C_3 [74]. The author assumes that it is just this which determines the function of these compounds as recognition pheromones.

In addition to compound (88), another two analogous monohydric trinervitane alcohols are known, having the structures (97) and (98). The first of them was isolated by Prestwich [75] from *Trinervitermes gratiosus*. The author notes the presence of this alcohol in only one of

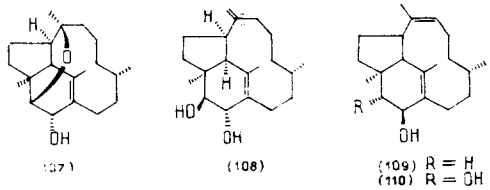
the three populations of termites studied, which indicates the chemotaxonomic value of the trinervitanoids for these insects.



The alcohol (98), however, the structure of which was established by the use of x-ray structural analysis, has been found in two other species of termites — *Trinervitermes trinervis* and *Trinervitermes occonomus* [76].

In the Malayan termites *Nasutitermes havilandi* Prestwich [77] found two propionate esters [(99) and (100)]. The structure of the triol (101), obtained on their saponification was established by x-ray structural analysis. The positions of the acyl residues and their molecules were established on the basis of partial saponification.

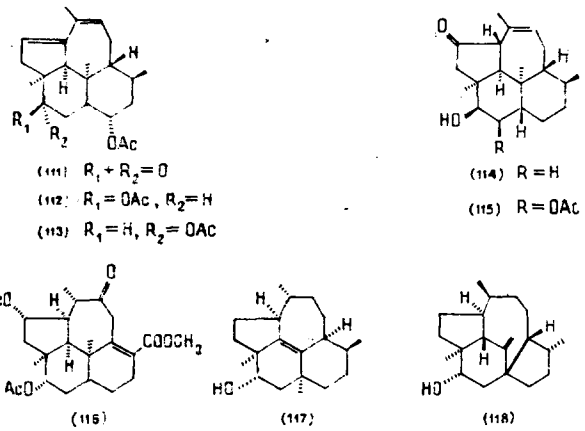
The diversity of natural trinervitanoids is illustrated by the work of Dupont [78] and Braekman [79]. The former found in four species of New Guinea termites 17 diterpenoids, five of which proved to be new [formulas (102)-(106)], and the latter isolated from the West African species *Nasutitermes lujae* four new triterpenoids having the structures expressed by formulas (107)-(110).



Tetracyclic Cyclocembranoids

The tetracyclic diterpenoids of termites are represented at the present time by six kempane derivatives and two compounds related to them. The first kempane diterpenoid, having the formula (111), was isolated by Prestwich [80] from *Nasutitermes kempae*. Its structure was established by x-ray structural analysis, and its absolute configuration on the basis of the sign of the Cotton effect for the π–π^* transition in the conjugated dienic system.

The same compound and two epimeric acetates (112) and (113) were isolated from the Malayan termites *Bulbitermes singaporensis* [81]. The structures of the latter were established on the basis of spectral characteristics.



The two keto derivatives (114) and (115) were isolated by Prestwich [82] from *Nasutitermes octopilis*. The structure of compound (114) was established by the x-ray structural analysis of its p-bromobenzoate, and that of the second compound on the basis of its PMR spectrum.

The most complex kempone derivative — the methyl ester of a diacetoxy acid having formula (116) — was found in *Nasutitermes costalis* [83]. Its structure was established by x-ray structural analysis.

Two diterpenoids with different carbon skeletons — 3-hydroxyrippert-15-ene (117) and longip-15(17)-en-3-ol (118) — have been isolated from *Nasutitermes rippertii* [84] and *Longipeditermes longipe* [71], respectively. The structure of the first was established by x-ray structural analysis and that of the second on the basis of two-dimensional NMR.

The rippertane derivative (117) is formed, as Prestwich et al. [84] assume by the migration of a methyl group in the molecule of a kempane precursor, and the longipane derivative by the cyclization of a trinervitadiene alcohol.

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