Marine Natural Products

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Reviewing the literature published between December 1987 and December 1988
(Continuing the coverage of literature in *Natural Product Reports*, 1988, Vol. 5, p. 613)

1 Introduction

This Report is a review of the literature of marine natural product chemistry for the period 1 December 1987 to the end of 1988. This is the sixth in a series of reviews published in *Natural Product Reports*. The earlier reports[1—5] cover the period from 1977 to December 1987.

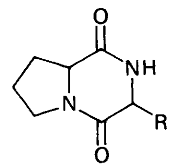
Like the earlier reports in this series, this review does not provide a comprehensive coverage of all research involving chemicals from marine organisms but concentrates on papers that report novel marine natural products with interesting biological and pharmaceutical properties. Biochemical studies involving marine organisms and reports of primary metabolites have been specifically omitted. Research on the biosynthesis of marine natural products has been reviewed in an excellent Report by Garson.[6] Owing to an expansion of interest in the pharmacological properties of marine natural products, it has become much more difficult to track the literature in this area. While every effort has been made to record the pharmacological activity of new metabolites, studies of mechanisms of action and reports of basic pharmacology in which marine natural products were used as biological probes are reviewed only when they result in a significant change in the biomedical status of a compound. In the area of synthetic organic chemistry, reports of the total synthesis of marine natural products or close analogues are included but papers dealing with methodology directed toward the synthesis of marine natural products have been omitted. No attempt has been made to review the patent literature or conference abstracts and reports.

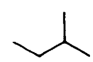
During the reporting period two volumes of a new series of interpretive reviews have appeared. The subjects covered in the review chapters are 'Natural Product Chemistry and Chemical Defense in Tropical Marine Algae of the Phylum Chlorophyta',[7] 'Chemical Ecology of the Nudibranchs',[8] 'Marine Metabolites which Inhibit Development of Echinoderm Embryos',[9] 'The Search for Antiviral and Anticancer Compounds from Marine Organisms',[10] 'Chemistry of Aqueous Marine Extracts: Isolation Techniques',[11] 'Secondary Metabolites from Echinoderms as Taxonomic Markers',[12] 'The Chemical Ecology of Alcyonarian Corals',[13] and 'Chemical Defense in Fishes'.[14]

2 Marine Microorganisms and Phytoplankton

Although there is considerable interest in the potential of marine bacteria and fungi to produce pharmacologically valuable compounds, very little activity has been reported in this field. It has been demonstrated that the three diketopiperazines (1)—(3) that were previously ascribed to the sponge *Tedania ignis*[15] are produced by a species of *Micrococcus* isolated from the sponge.[16] Dendryphiellin A (4) is an unprecedented metabolite, of possible terpenoid origin, from the marine deuteromycete *Dendryphiella salina*.[17]

Interest in the dinoflagellates arises primarily from their implication in outbreaks of ciguatera poisoning, an illness caused by ingestion of reef fishes. The dinoflagellate most commonly associated with ciguatera outbreaks in the Pacific is *Gambierdiscus toxicus*, from which the partially characterized maitotoxin was isolated.[18] A new nitrogenous toxin called prorocentrolide (5) was isolated from *Prorocentrum lima*,[19]



(1) R = 
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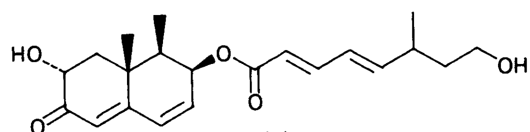
(3) R = Me



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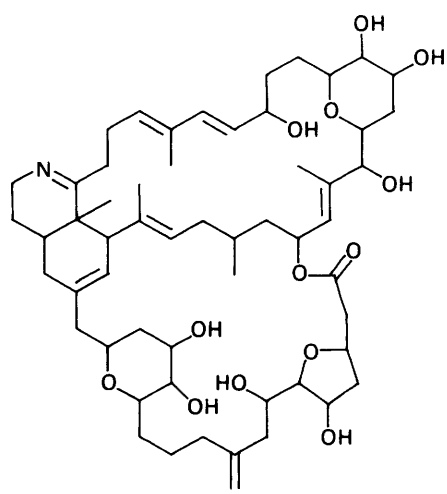

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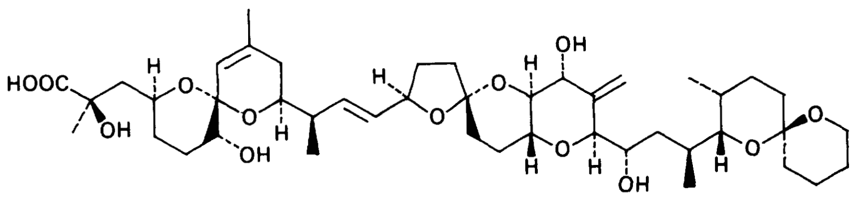

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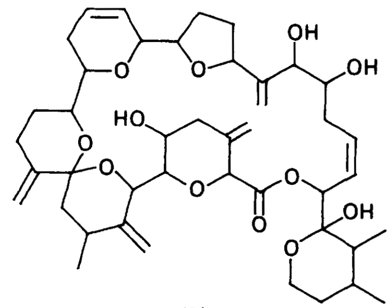

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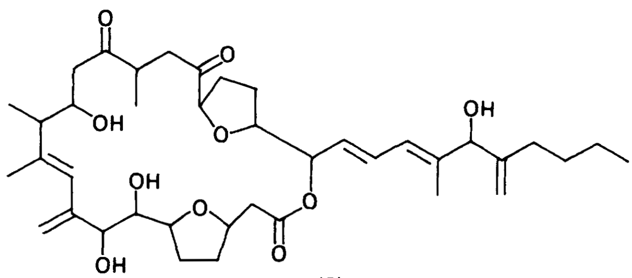

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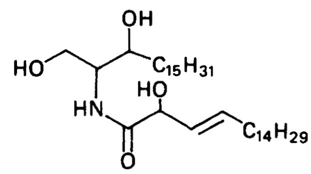

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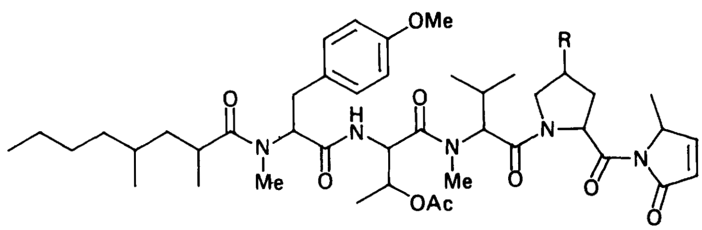

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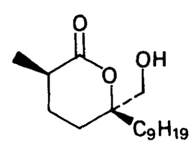

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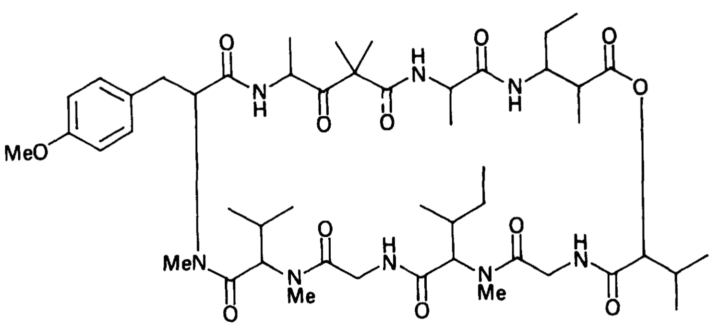

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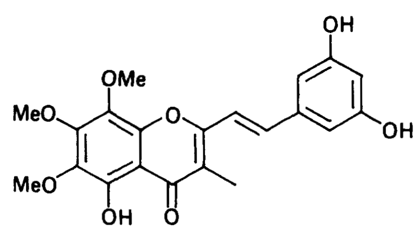

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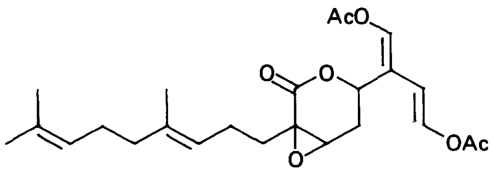
from which the structurally unrelated toxin okadaic acid (6) had previously been obtained.[20] The stereochemistry of prorocentrolide (5) remains to be determined as does that of the antifungal agent goniodomin A (7), which was isolated from *Goniodoma pseudogoniaulax*.[21] Amphidinolide C (8) is a 25-membered macrocyclic lactone from a cultured dinoflagellate of the genus *Amphidinium* that was originally obtained from a flatworm.[22] Like previous compounds from this source,[23,24] amphidinolide C (8) has potent antineoplastic activity. The sphingosine derivative symbioramide (9), which was isolated from the cultured species of *Symbiodinium*, is an activator of sarcoplasmic reticulum Ca^{2+}-ATPase.[25]

3 Blue-Green Algae (Cyanobacteria)

The majority of studies during the past year have featured terrestrial rather than marine cyanophytes. The exceptions are reports of the isolation and structural elucidation of two cytotoxic linear pentapeptides, majusculamide D (10) and deoxymajusculamide D (11),[26] and a minor cyclic depsipeptide, 57-normajusculamide C (12),[27] from *Lyngbya majuscula*. A new synthesis of (−)-malyngolide (13), which is a metabolite of *Lyngbya majuscula*,[28] employed an asymmetric reduction using Baker's yeast.[29] The cytotoxic styrylchromone hormothamnione (14), that was isolated from *Hormothamnion enteromorphoides*,[30] has been synthesized by two similar routes.[31,32]



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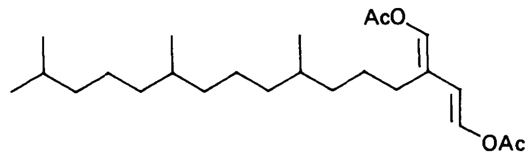

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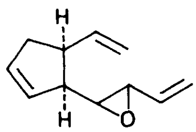

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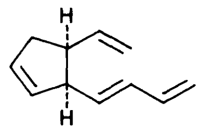

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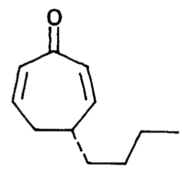

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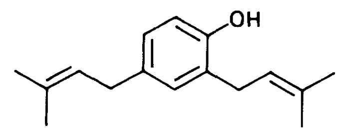

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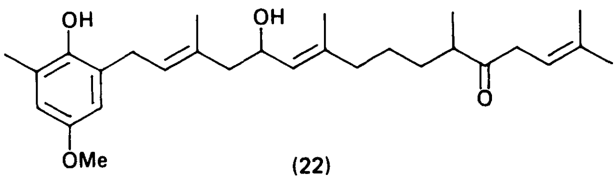

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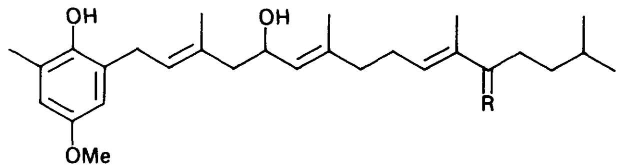
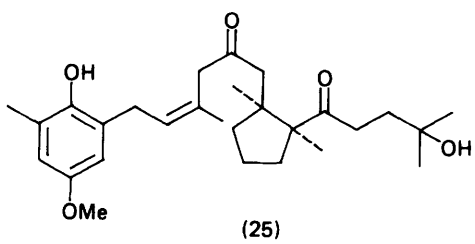


(23) R = O

(24) R = H,OH



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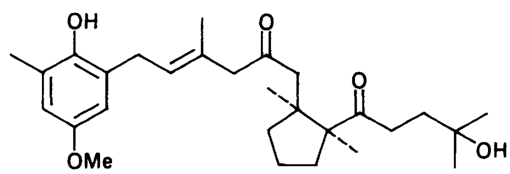

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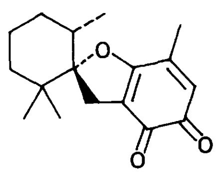

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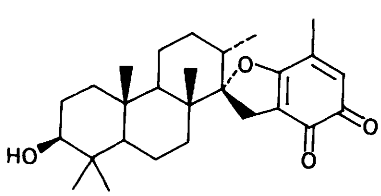

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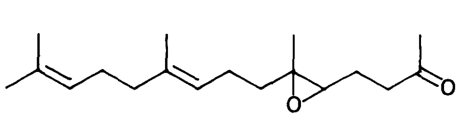
4 Green Algae

The chemical defences of tropical green algae continue to be studied in detail,[7,33] but few new metabolites have been described. The only exceptions are two new diterpenoid fish-feeding inhibitors (15) and (16) from *Pseudochlorodesmis furcellata*.[34]

5 Brown Algae

A review of 'The odoriferous polyene hydrocarbons from marine and terrestrial plants' provides a compact account of research on the pheromones of marine brown algae.[35] Caudoxirene (17) is a new spermatozoid-releasing and attracting factor from *Perithalia caudata*.[36] The structure of caudoxirene (17) was determined by GC-mass spectral analysis coupled with micro-scale deoxygenation to obtain *E*-viridiene (18) and was confirmed by synthesis. Five species of brown algae from Victoria, Australia, all use slightly different enantiomeric compositions of (−)-1*R*,2*R* hormosirene (19) and (+)-1*S*,2*S* hormosirene as gamete attractants.[37] (*R*)-(+)-4-Butyl-2,6-cycloheptadienone (20), which is a minor constituent of the essential oil of a Hawaiian species of *Dictyopteris*,[38] was synthesized in good yield by a route that employed a ring expansion to construct the 7-membered ring.[39]

GC–MS analysis of the constituents of the Australian algae *Zonaria turneriana*, *Z. crenata*, and *Z. angustata* revealed only known acylphloroglucinol derivatives.[40] A second diprenylphenol (21) was found in *Perithalia caudata* from Australia.[41] Three new tetraprenyltoluquinols (22)—(24) were isolated from a Sicilian species of *Cystoseira*.[42] A natural hybrid between *Cystoseira elegans* and *C. algeriensis*, previously reported as *C. algeriensis*,[43,44] has been described together with the structural elucidation of two new tetraprenyltoluquinols (25) and (26).[45] A model compound (27) incorporating the active portion of the cytotoxin stypoldione (28)[46] has been synthesized.[47]



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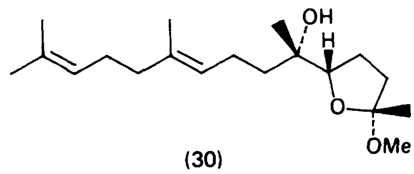

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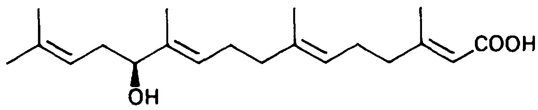

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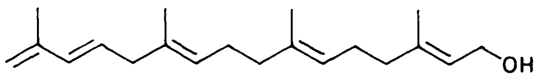

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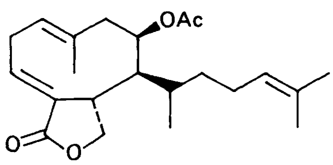

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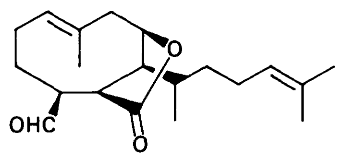

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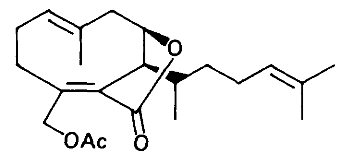

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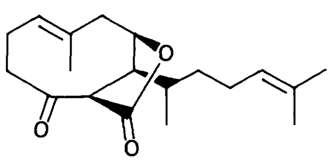

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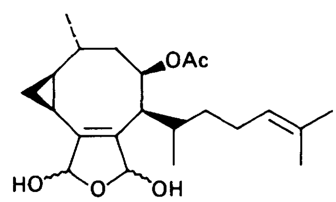

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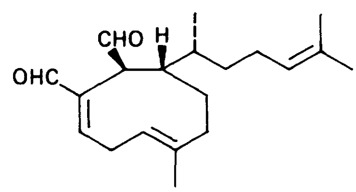

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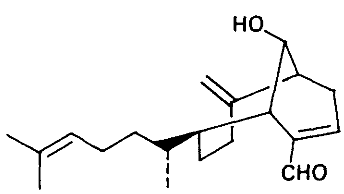

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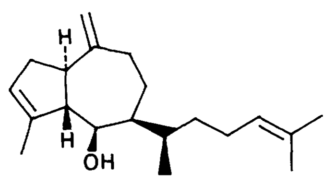

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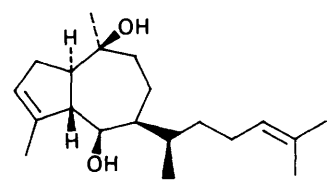

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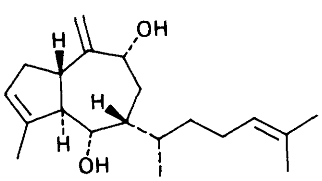

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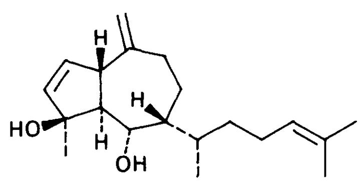

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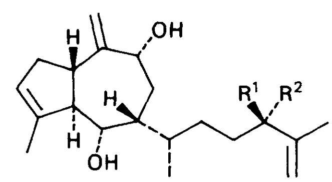
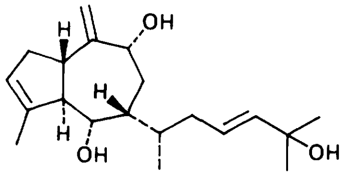


(44) $R^1 = OH$, $R^2 = H$
(45) $R^1 = H$, $R^2 = OH$

A reinvestigation of *Cystophora moniliformis* resulted in the isolation of two new terpenoids (29) and (30)[48] in addition to those metabolites reported previously.[49,50] The methyl acetal (30) is believed to arise by methanolysis of the epoxide (29) during chromatography. Two additional acyclic diterpenes (31) and (32) have been reported from *Bifurcaria bifurcata*.[51] Three new diterpenes of the xenicane class, 4-acetoxydictyolactone (33) and dictyolides A (34) and B (35), together with a norxenicane derivative, nordictyolide (36), are the antitumour constituents of *Dictyota dichotoma* from Okinawa.[52] The conformations of these interesting bicyclic diterpenes were determined by interpretation of 2D-NOESY experiments. The structure of crenuladial (37), which is an antimicrobial diterpenoid from *Dilophus ligatus*, is actually a mixture of bis-hemiacetals resulting from hydration of a hypothetical 1,4-dialdehyde.[53] The absolute configurations of dictyodial (38), originally isolated from *Dictyota crenulata*,[54] and the bicyclic isomer sanadaol (39) from *Pachydictyon coriaceum*[55] were determined by an enantioselective synthesis of both (+)- and (−)-sanadaol.[56] In addition to the known diterpenes (40)—(43),[57—60] three new hydroazulenoid diterpenes, dictyotriols C (44), D (45) and E (46), were obtained from a Canary



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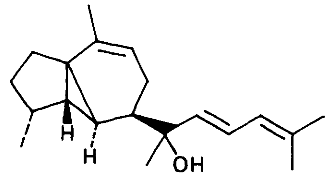

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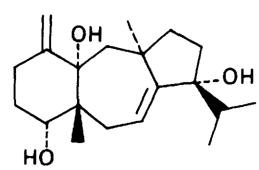

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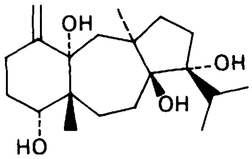

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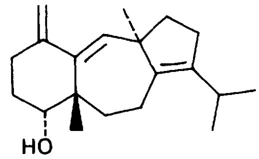

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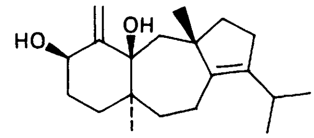

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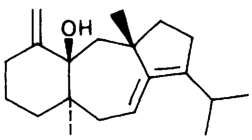

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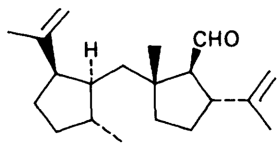

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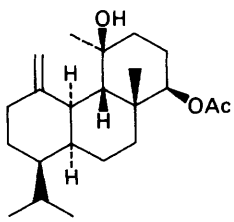

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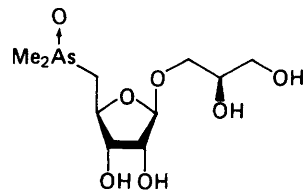

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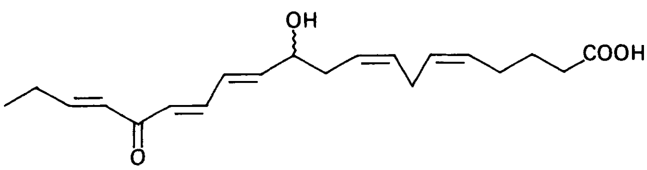

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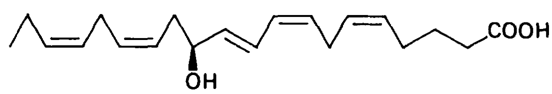

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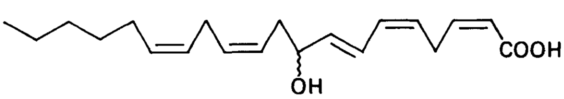

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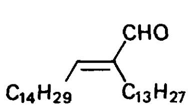


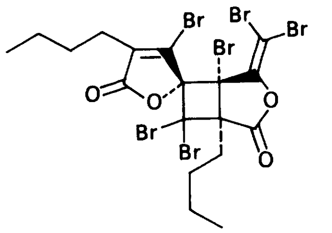
(59)

Islands species of *Dictyota*. [61] The absolute configurations of the new compounds (44)—(46) and those of dictyol B (41) and dictyotadiol (43) were determined by the CD allylic benzoate method and were found to be opposite to that determined for pachydictyol A (40) by *X*-ray crystallography.[57] The novel tricyclic diterpene (47) from *Dilophus okamurai* inhibits feeding by young abalone.[62] Two new dolastane diterpenes (48) and (49) have been isolated from *Dictyota cervicornis* from Brazil.[63] Amijitrienol (50), which is a metabolite of *Dictyota linearis*,[64] has been synthesized in racemic form by a 10-step sequence.[65] Both (+)-isoamijiol (51) and (+)-dolasta-1(15),7,9-trien-14-ol (52), which are optical enantiomers of the natural products,[66,67] have been synthesized from (+)-limonene.[68] The unusual diterpenoid dictymal (53), which is a metabolite of *Dictyota dichotoma*,[69] has been synthesized from two optically active iridoid (monoterpene) synthons.[70] One of the more unusual compounds from a Canary Islands species of *Dictyota* is β-dictalediol monoacetate (54), the structure of which was determined by *X*-ray analysis.[71]

The arsenic-containing carbohydrate (55), which was isolated from the kelp *Ecklonia radiata*,[72] has been synthesized from D-ribose.[73]

6 Red Algae

The eicosanoids, which are a family of biologically active arachidonic acid derivatives, are fairly frequently found in extracts of marine organisms. Ptilodene (56) is an eicosanoid from *Ptilota filicina* that inhibits both 5-lipoxygenase and Na^+/K^+ ATPase.[74] 12-(*S*)-Hydroxyeicosapentaenoic acid (57), which is a potent inhibitor of platelet aggregation, has been isolated in large quantities from *Murrayella periclados* and has been recognized as the compound previously identified[75] as 9-hydroxypentaenoic acid (58) from *Laurencia hybrida*.[76] The unusual unsaturated aldehyde, (*E*)-2-tridecyl-2-heptadecenal (59), was isolated from a Japanese species of *Laurencia* and was synthesized by aldol dimerization of pentadecanal.[77] Six new



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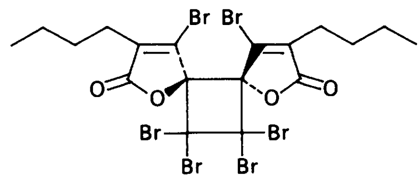

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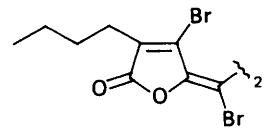

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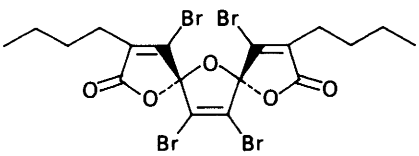
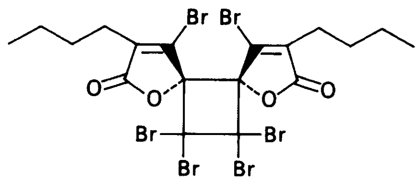


(63)



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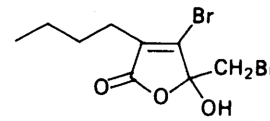

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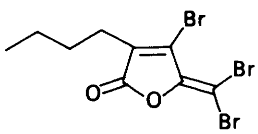
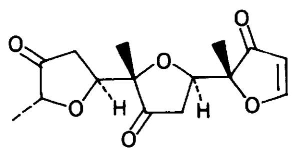


(66)



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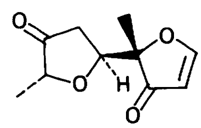

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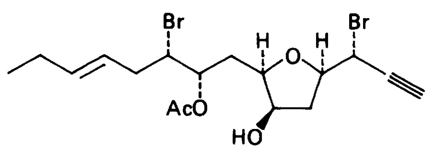

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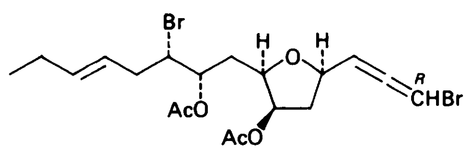

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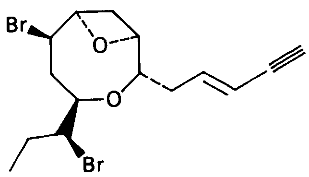

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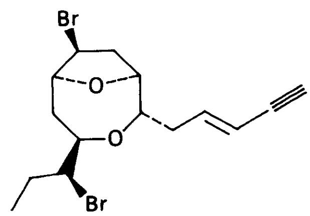

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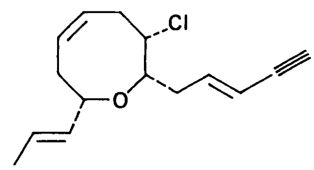
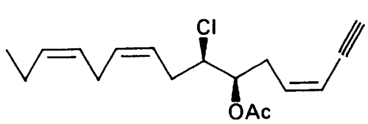


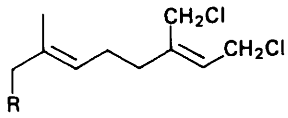
(73)



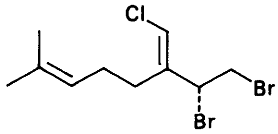
(74)

polybrominated 2(5*H*)-furanones (60)—(65) have been isolated from *Delisea elegans*.[78] Five of the new compounds may be considered as dimers of the fimbrolide (66) that was previously isolated from *Delisea fimbriata*.[79] The structures of dimers (60)—(63) were all determined by *X*-ray studies and the remaining compounds were identified by interpretation of spectral data. Chilenone B (67) is an unusual trimer of 2-methyl-3(2*H*)-furanone that was isolated in low yield from *Laurencia chilensis*.[80] The structures of chilenones A (68)[81] and B (67), both of which were established by *X*-ray analysis, are totally unrelated to other *Laurencia* metabolites.

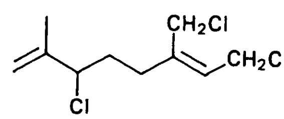
A new halogenated C_{15} acetylene, graciosin (69), and the corresponding allene, graciosallene (70), were obtained from a Canary Island specimen of *Laurencia obtusa* and the structures were determined by *X*-ray crystallography and chemical methods.[82] The known compounds (3*E*)-laureatin (71) and (3*E*)-isolaureatin (72)[83] have been reported as the major constituents of a specimen of *Laurencia nipponica* from Shichigahama, Japan.[84] (−)-Laurenyne (73) has been synthesized using an acetal-initiated cyclization to form the crucial 8-membered ring.[85] This synthesis served to redefine the absolute configuration of (+)-laurenyne, which had earlier been determined by *X*-ray analysis of material obtained from an Aegean Sea specimen of *Laurencia obtusa*.[86] The enantioselective syntheses of (3*Z*,6*R*,7*R*,9*Z*,12*Z*)-6-acetoxy-7-chloropentadeca-3,9,12-trien-1-yne (74) and the corresponding (3*E*) isomer, which are metabolites of *Laurencia pinnatifida*,[87] have been reported.[88]



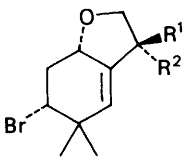
(75) R = Cl
(76) R = H



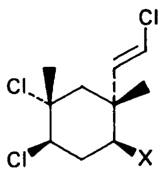
(77)



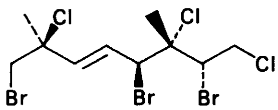
(78)



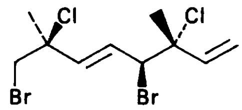
(79) R^1 = Cl, R^2 = H
(80) R^1 = H, R^2 = Cl



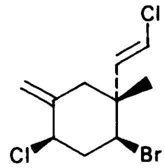
(81) X = Cl
(85) X = Br



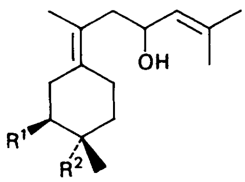
(82)



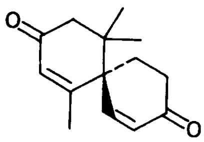
(83)



(84)



(86) R^1 = Br, R^2 = Cl
(87) R^1 = Cl, R^2 = Br



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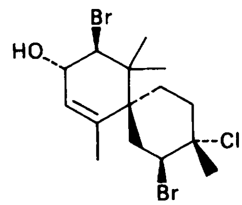

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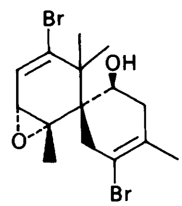

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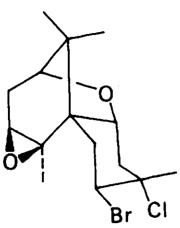

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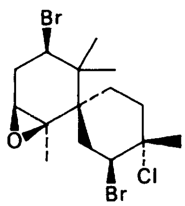

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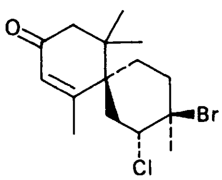
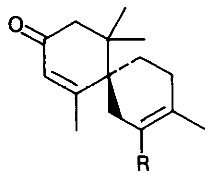
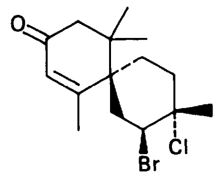


(93)



(94) R = Cl
(95) R = H



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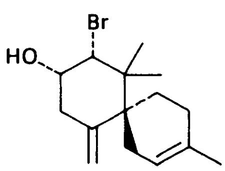
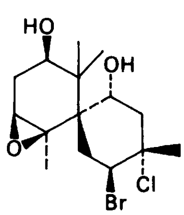


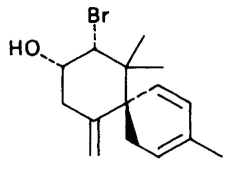
(97)



(98)

Four polyhalogenated linear monoterpenes (75)—(78) and two epimeric bicyclic monoterpenes (79) and (80) were isolated from a Great Barrier Reef sample of *Chondrococcus hornemannii* and their structures were elucidated by interpretation of spectral data.[89] Four new polyhalogenated monoterpenes (81)—(84) have been found in two collections of *Plocamium hamatum* from Australia. One collection contained the cyclic monoterpene (81), which is closely related to the known metabolite mertensene (85),[90] while the second collection contained two linear monoterpenes (82) and (83) and one cyclic monoterpene (84).[91] The distribution of aromatic sesquiterpenes in several species of *Laurencia* from the South Australia coast has been reported but no new compounds were encountered.[92]

Puertitols A (86) and B (87) are novel halogenated bisabolenes from a Canary Islands sample of *Laurencia obtusa*.[93] The structures were elucidated by interpretation of spectral data and the absolute configurations determined by use of the CD allylic benzoate method. Majusculone (88) is an unusual norchamigrene derivative from *Laurencia majuscula* collected in Japan.[94] The structure of 2,10-dibromo-3-chamigren-7-en-9-ol (89), previously reported as a metabolite of *Laurencia pacifica*[95] and now found in *Laurencia nipponica*, has been confirmed and the absolute configuration determined by *X*-ray analysis.[96] A new labile sesquiterpene, dehydrochloroprepacifenol (90), has been obtained from a Mediterranean specimen of *L. majuscula*.[97] The structure of (90) was determined by low-temperature *X*-ray diffraction analysis. Pinnatazane (91), the structure of which was determined by *X*-ray analysis, is a new chamigrene derivative from *L. pinnatifida*.[98] The known epoxide (92), previously reported from an unidentified species of *Laurencia*,[99] has also been reported from *L. pinnatifida*.[100] Five new chamigrene derivatives, laurencenones A—D (93)—(96) and deschloroelatol (97), were obtained from a Jamaican specimen of *L. obtusa*.[101] A specimen of *L. scoparia* from Jamaica contained several known chamigrenes and the novel epoxide (98).[101] The structures of all new compounds were determined by interpretation of spectral data. Two new



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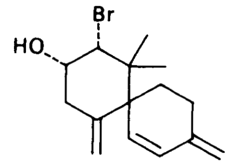

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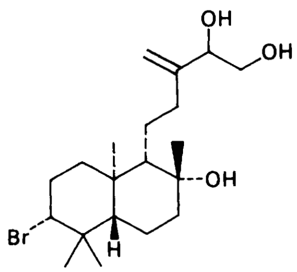

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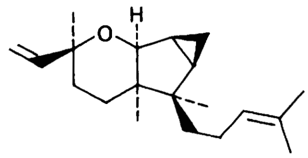

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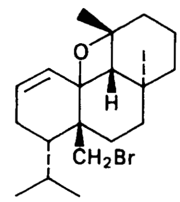

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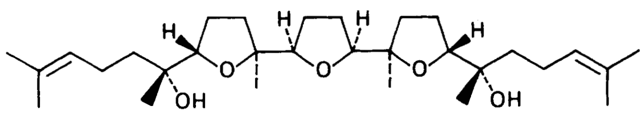

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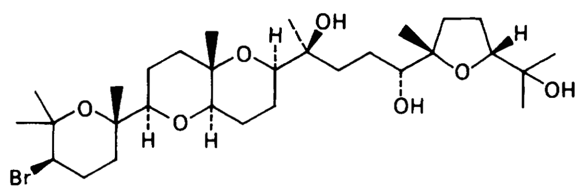

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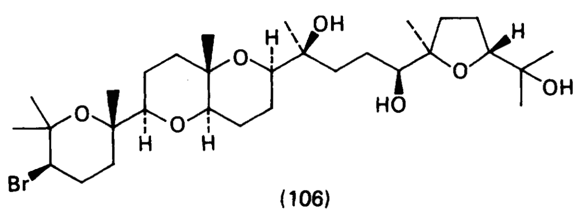

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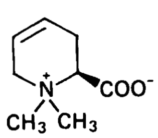

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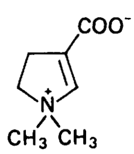

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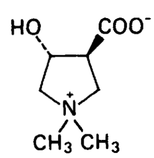

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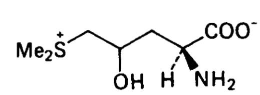

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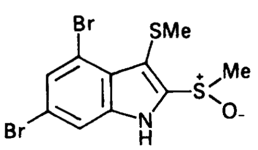

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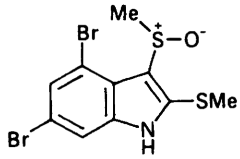


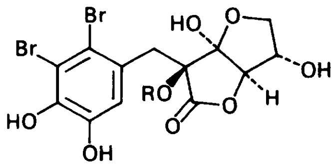
(112)

chamigrenes, obtusadiene (99) and isoobtusadiene (100), were isolated from a Puerto Rican specimen of *L. obtusa*; the structures were elucidated by analysis of spectral data and the absolute stereochemistry was defined by using the CD benzoate method.[102]

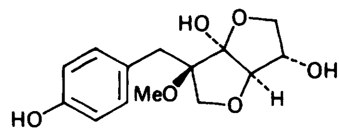
Venustanol (101) is a brominated labdane diterpene from *Laurencia venusta* that was identified by spectral methods.[103] Two new brominated diterpenes, sphaeropyrane (102)[104] and sphaeroxetane (103),[105] have been recognized as minor metabolites of *Sphaerococcus coronopifolius* and their structures have been proposed on the basis of spectral data.

The triterpenes from *Laurencia* species have been the targets of five synthetic efforts. Teurilene (104), which is a metabolite of *Laurencia obtusa*,[106] has been synthesized by two very similar routes.[107,108] Two syntheses of venustatriol (105) from *L. venusta*[109] and one synthesis of thyrsiferol (106) from *L. thyrsifera*[110] have been reported.[111–113] These routes all involve the formation of cyclic ethers through reactions involving the reaction of alcohols with epoxides.

The red algae often contain unusual amino acids. Recent examples are the quaternary ammonium compounds (107) and (108) from *Pterocladia capillacea*[114] and (109) from *Grateloupia proteus*,[115] and the dimethyl sulphonium salt (110) from *Lophocladia lallemandi*.[115] Itomanindoles A (111) and B (112)



(113) R = H
(114) R = Me



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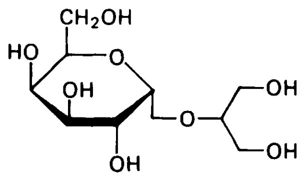
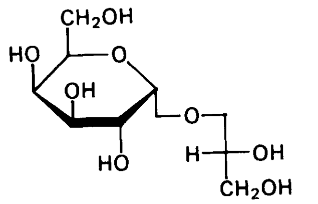
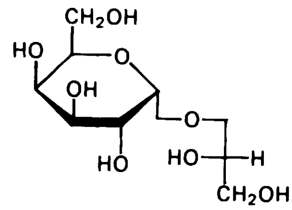


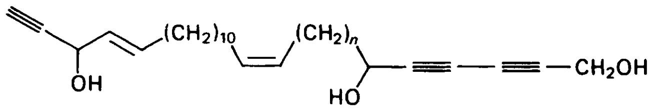
(116)



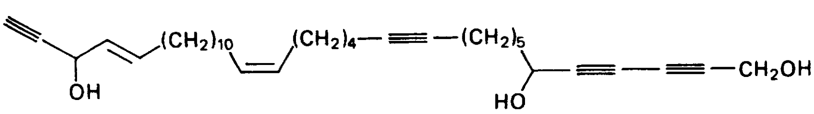
(117)



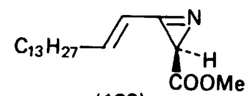
(118)



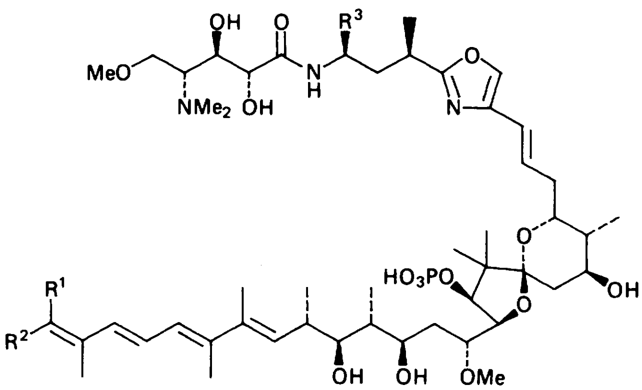
(119) n = 10
(120) n = 9



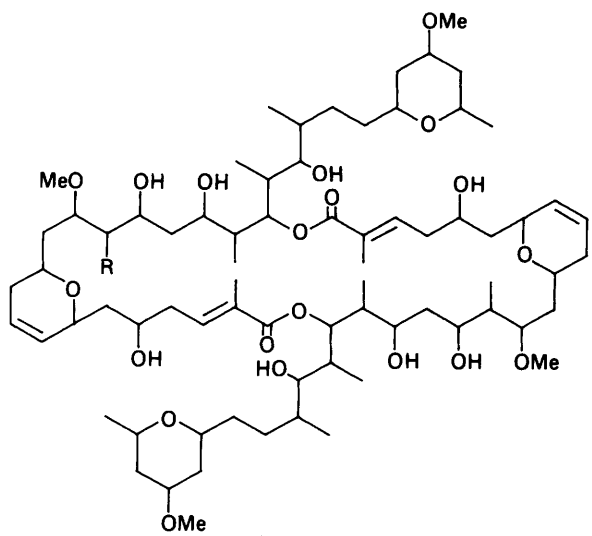
(121)



(122)



(123) R^1 = H, R^2 = CN, R^3 = H
(124) R^1 = CN, R^2 = H, R^3 = Me
(125) R^1 = H, R^2 = CN, R^3 = Me
(126) R^1 = CN, R^2 = H, R^3 = H

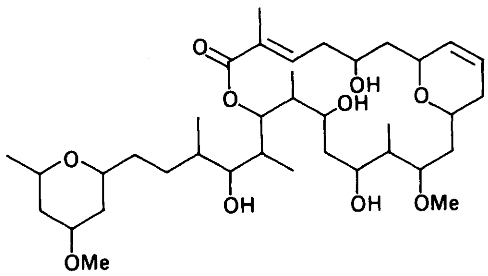


(127) R = Me
(128) R = H

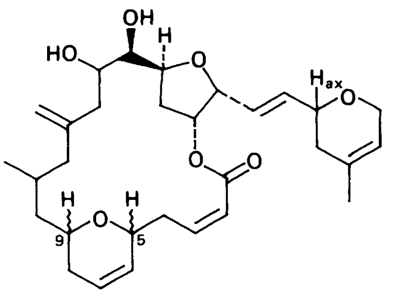
are two isomeric methylsulphinyl substituted indoles from *Laurencia brongniartii*.[116] The structure of itomanindole A (111) was determined by *X*-ray analysis. Two phenolic metabolites of *Polysiphonia lanosa*, rhodomelol (113) and methylrhodomelol (114),[117] and delesserine (115), which was obtained from *Delesseria sanguinea*,[118] have been synthesized from vitamin C.[119] Floridoside (116), 'D'-isofloridoside (117) and 'L'-isofloridoside (118) have been characterized as metabolites of *Porphyra perforata*.[120]

7 Sponges

Three new polyacetylenic alcohols, melynes A (119), B (120) and C (121), have been isolated from a species of *Xestospongia* from Vanuatu.[121] The structures of the melynes were elucidated from spectral data. Melyne A (119) is active against the intestinal protozoan *Giardia*. Dysidazirine (122) is a unique azacyclopropene-containing lipid from *Dysidea fragilis*.[122] The structure of dysidazirine (122), which is cytotoxic and inhibits *P. aeruginosa*, *C. albicans*, and *S. cerevisiae*, was elucidated by chemical and spectroscopic methods. *Discodermia calyx* has yielded three new cytotoxins – calyculins B (123), C (124), and D (125) – that were identified by comparison of spectral data with those of the known[123] metabolite, calyculin A (126).[124] Two cytotoxic macrodiolides (dimeric macrolides), bistheonellides A (127) and B (128), have been isolated from a Japanese species of *Theonella*.[125] Bistheonellide A (127) was shown to be identical to misakinolide-A, for which the incorrect

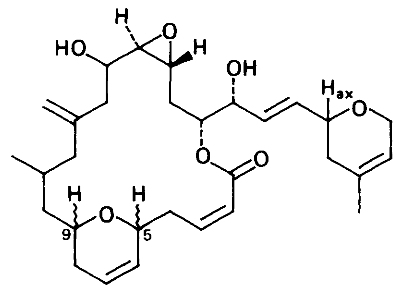


(129)



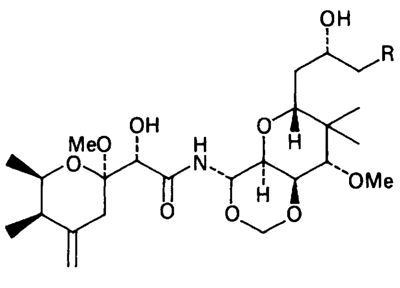
(130) ax H-5, eq H-9

(132) eq H-5, ax H-9



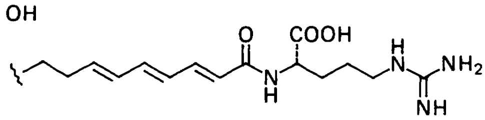
(131) ax H-5, eq H-9

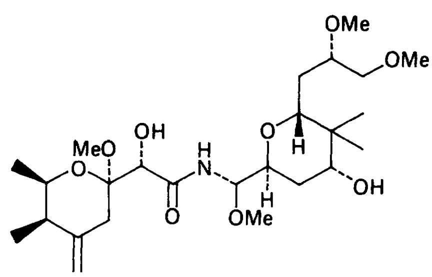
(133) eq H-5, ax H-9



(134) R = OH

(135) R =

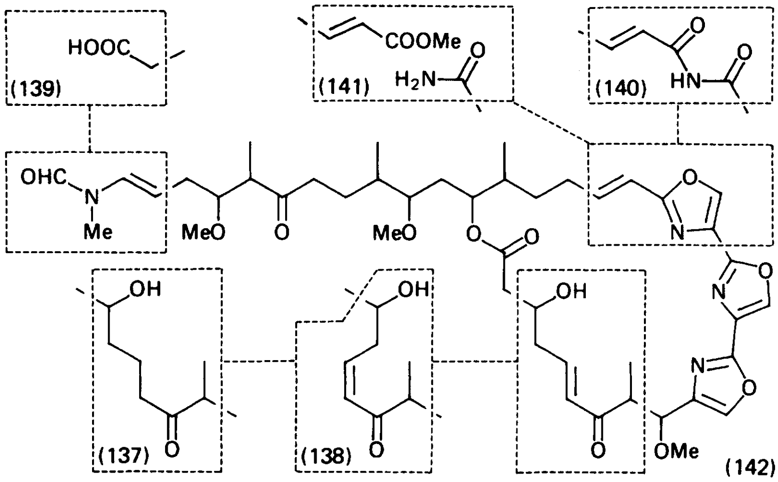




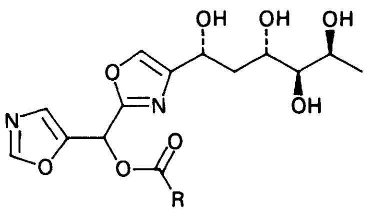
(136)

monomeric structure (129) had earlier been proposed.[126] It is not immediately clear whether fijianolides A (130) and B (131), isolated from *Spongia mycofijiensis* from Vanuatu,[127] are identical to isolaulimalide (132) and laulimalide (133), respectively, from an Indonesian species of *Hyatella*.[128] The spectral data for these cytotoxic metabolites were reported in different solvents making direct comparisons impossible and the proposed structures differ in the conformation assigned at C-5 and C-9, It is hoped that a future paper will resolve this confusion and report the complete stereochemical assignment for these interesting metabolites. A new group of antiviral compounds have been isolated from two unrelated sponges. Mycalamide A (134), which is a metabolite of a New Zealand species of *Mycale*,[129] and onnamide A (135), which occurs in an Okinawan species of *Theonella*,[130] differ only in the size and nature of the side chain and both compounds resemble pederin (136), which was isolated from a terrestrial beetle *Paederus fuscipes*.[131] The structures of mycalamide A (134) and onnamide A (135) were elucidated by interpretation of spectral data and the stereochemistry has been assumed to be the same as that of pederin (136).

A species of *Halichondria* from Palau contained five minor macrolides (137)—(141) in addition to the major metabolite halichondramide (142) that was reported previously,[132] The structures of dihydrohalichondramide (137), isohalichondramide (138), acid (139), imide (140), and ester (141) were determined by comparison of the spectral data with those of halichondramide (142).[133] Two unusual anthelmintic oxazoles, bengazoles A (143) and B (144), have been isolated from a Fijian sponge of the family Jaspidae.[134] The structures proposed for the bengazoles were based on a detailed analysis of ^{1}H NMR data, assisted by molecular modelling. Mycothiazole (145) is a novel thiazole-containing lipid with anthelmintic properties that was isolated from *Spongia mycofijiensis*.[135] The structure of mycothiazole (145) was established by analysis of spectral data.

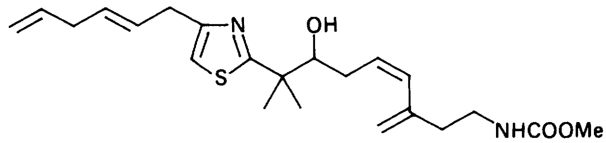


(142)

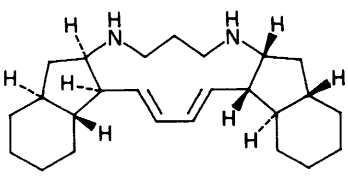


(143) R = $(CH_2)_{12}CH_3$

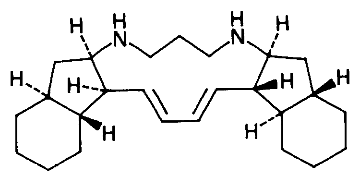
(144) R = $(CH_2)_{11}CH(CH_3)_2$



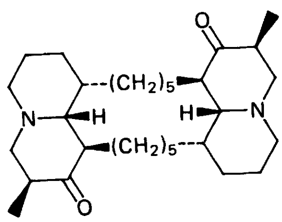
(145)



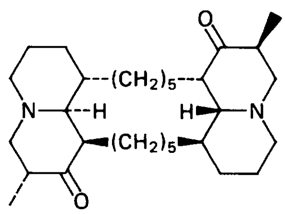
(146)



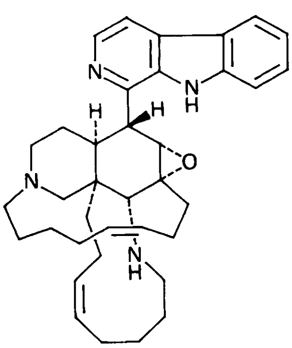
(147)



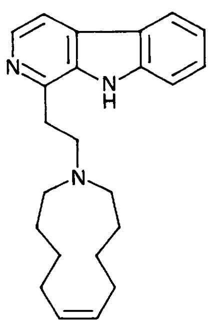
(148)



(149)

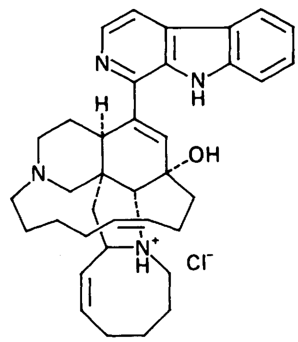


(150)

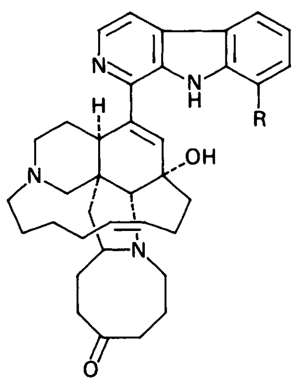


(151)

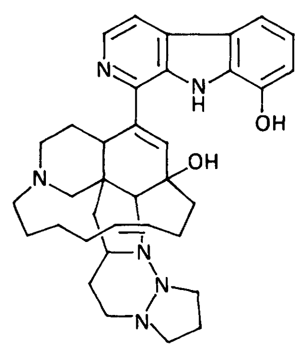
An unusually large number of alkaloids have been reported from sponges during the current review period. The antifungal alkaloid papuamine (146) was isolated from a Papua New Guinea specimen of *Haliclona* and its structure was elucidated by analysis of spectral data.[136] The same compound was found to be a minor constituent of a Palauan species of *Haliclona* (*cf. H. hornelli*) that contained haliclonadiamine (147), which is an unsymmetrical diastereoisomer of papuamine (146), as the major antifungal metabolite.[137] The structure of haliclonadiamine (147) was determined by *X*-ray analysis. The structure of petrosin-A has been revised from (148) to (149) as the result of a 2D-NMR study.[138] Four new alkaloids of the manzamine family have been reported from sponges of the genus *Haliclona* and *Xestospongia*. Manzamines B (150) and C (151) were



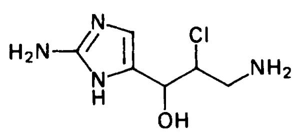
(152)



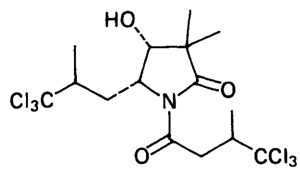
(153) R = H
(154) R = OH



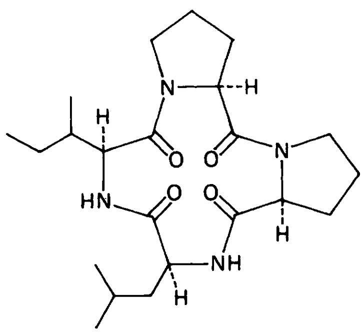
(155)



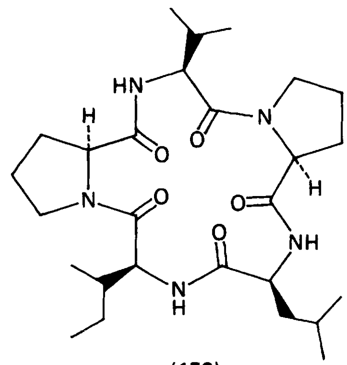
(156)



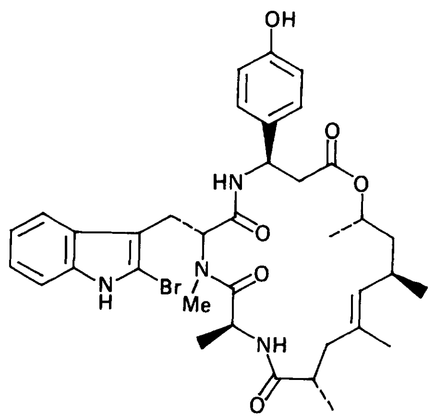
(157)



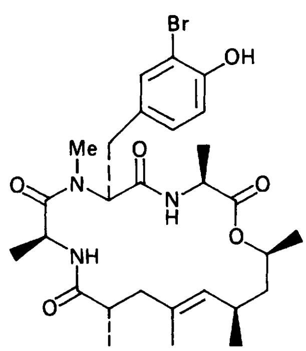
(158)



(159)



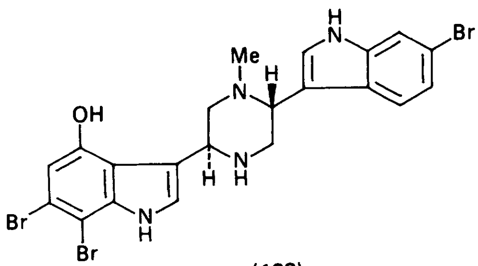
(160)



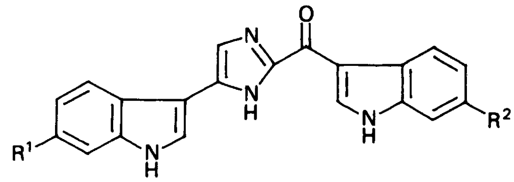
(161)

obtained along with the known alkaloid manzamine A (152)[139] from an Okinawan species of *Haliclona*.[140] The structures of both new alkaloids were determined by *X*-ray analysis. Manzamines E (153) and F (154), which are the cytotoxic constituents of an Okinawan species of *Xestospongia*, were identified by comparison of their spectral data with those of manzamine A (152).[141] Manzamine F (154) was shown to be the same as an alkaloid called keramamine B, to which the incorrect structure (155) had been assigned.[142]

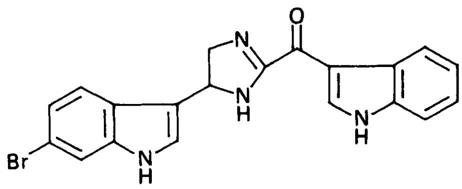
The cytotoxic alkaloid girolline (156) was isolated from the axinellid sponge *Pseudaxinyssa cantharella* from New Caledonia.[143] The structure of girolline was elucidated by physicochemical methods. Dysidamide (157) is a new hexachlorinated amino acid derived metabolite from a Red Sea species of *Dysidea*.[144] The structures of two new cyclic peptides, fenestrins A (158) and B (159), from the Fijian sponge *Leucophloeus fenestrata*, were proposed on the basis of spectral analysis.[145] The cyclic depsipeptides jaspamide (160), which is a metabolite of a species of *Jaspis*,[146,147] and geodiamolide B (161) from a species of *Geodia*[148] have been the subject of



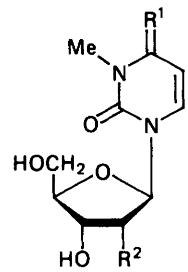
(162)



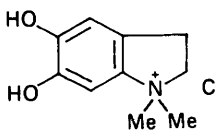
(163) R^1 = H, R^2 = OH
(164) R^1 = Br, R^2 = OH
(166) R^1 = H, R^2 = H



(165)



(167) $R^1 = \overset{+}{N}H_2$, R^2 = OH
(168) $R^1 = \overset{+}{N}H_2$, R^2 = H
(169) R^1 = O, R^2 = H



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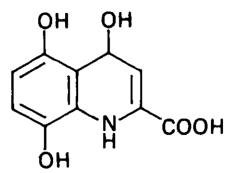
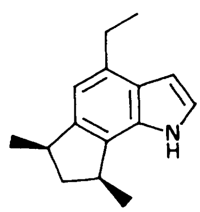
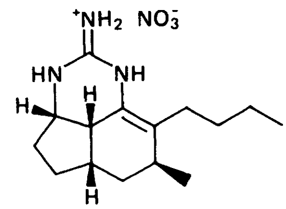


(171)



(172)



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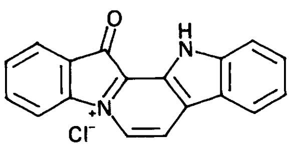
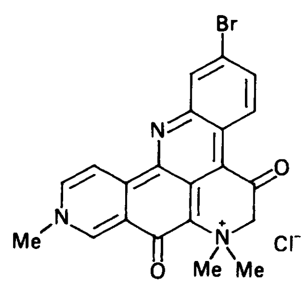


(174)

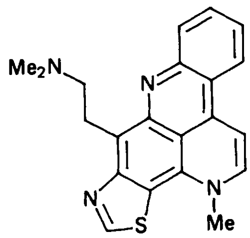


(175)

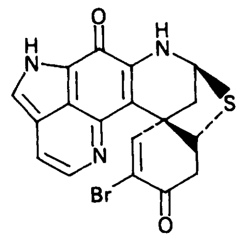
several synthetic efforts. Both the polypropionate[149] and the peptide[150] portions of jaspamide have been synthesized separately and total syntheses of both jaspamide (160)[151] and geodiamolide B (161)[152] have been reported.

Dragmacidin (162) is a cytotoxic bis-indole alkaloid from a deep-water species of *Dragmacidon*.[153] The structure of dragmacidin (162), which showed *in vitro* activity against P388 cells and against human lung, colon, and mammary cancer cell lines, was elucidated by interpretation of spectral data. Four species of *Spongosorites* collected in deep water off the Bahamas have yielded two known alkaloids, topsentins-B1 (163) and -B2 (164), that had previously been found in a Mediterranean shallow-water sponge called *Topsentia genitrix*,[154] together with a new alkaloid (165).[155] The synthesis of topsentin-B1 (163) and several analogues were reported, together with their antiviral and antitumour activities. A synthesis of topsentin-A (166), which is the simplest of the alkaloids from *T. genitrix*, has also been reported.[156] *T. genitrix* also contains the free base 3-methyladenine.[157] 3-Methylcytidine (167), 3-methyl-2′-deoxycytidine (168), and 3-methyl-2′-deoxyuridine (169) were identified as the metabolites of *Geodia baretti* that caused strong contractile activity in the guinea-pig ileum assay.[158] 1,1-Dimethyl-5,6-dihydroxyindolinium chloride (170) has been isolated from a deep-water species of *Dercitus*,[159] and 4,5,8-trihydroxyquinoline-2-carboxylic acid (171) was found to be the antimicrobial constituent of the Antarctic sponge *Dendrilla membranosa*.[160] The indole alkaloid trikentrin A (172), which was isolated from *Trikentrion flabelliforme*,[161] has been synthesized using pyrolysis of an azide to form the 'pyrrole' ring.[162] Ptilocaulin (173), which is a cytotoxic metabolite of *Ptilocaulis* aff. *P. spiculifer*,[163] has been synthesized in racemic form by using a photochemical rearrangement as the key step.[164]

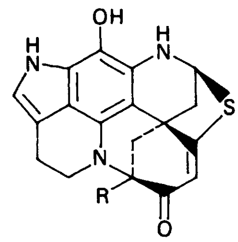
A number of polycyclic heteroaromatic pigments have been isolated from marine sponges. Since some of these pigments are remarkably similar to pigments found in other sessile marine organisms, it has been suggested (but not demonstrated) that they might all be produced by microbial symbionts. Fascaplysin (174) is an unusual antimicrobial pigment from a Fijian species of *Fascaplysinopsis*.[165] The colour of the pigment petrosamine (175), which was isolated from a Caribbean species of *Petrosia*, is dependent on the polarity of the solvent and varies from



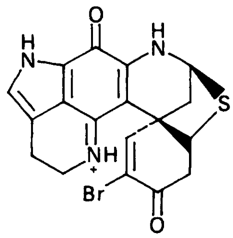
(176)



(177)



(178) R = OH
(179) R = H



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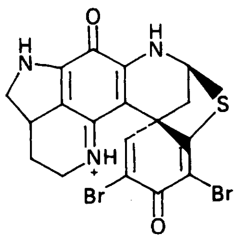

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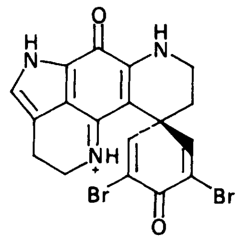

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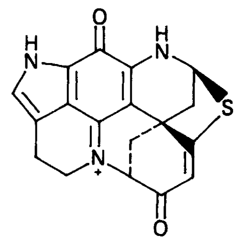

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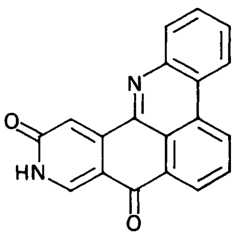

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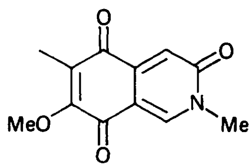

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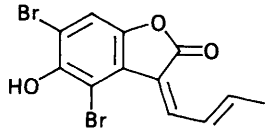

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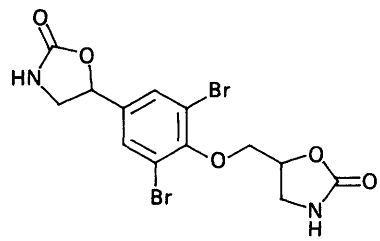
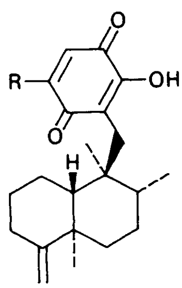
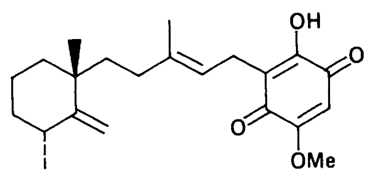


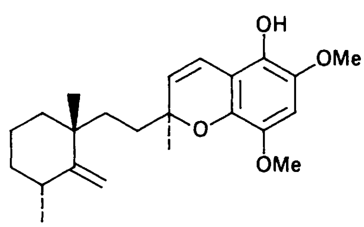
(187)



(188) R = OMe
(189) R = NH_2



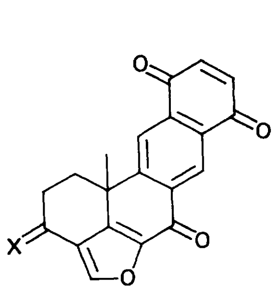
(190)



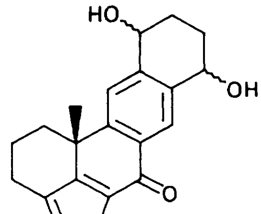
(191)

green (in THF) to purple (in water).[166] The structures of both fascaplysin (174) and petrosamine (175) were determined by *X*-ray analysis. Dercitin (176) is a violet pigment from a deep-water species of *Dercitus* that exhibits antitumour, antiviral and immunomodulatory properties *in vitro* and has *in vivo* antitumour activity.[167] The structure of this novel acridine alkaloid was proposed on the basis of its spectral properties. Prianosins B (177), C (178), and D (179) are sulphur-containing alkaloids from *Prianos melanos* that have potent antineoplastic activity.[168] The structures of prianosins B—D (177)—(179) were elucidated by interpretation of spectral data. Discorhabdins A (180), B (181), C (182), and D (183) are cytotoxic pigments from a New Zealand species of *Latrunculia*.[169,170] Discorhabdin D (183) has also been found in an Okinawan species of *Prianos*.[170] The structure of discorhabdin A (180) was identical to that previously reported for prianosin A[171] and the remaining discorhabdins were identified on the basis of spectral analysis. Amphimedine (184), which is a cytotoxic constituent of a species of *Amphimedon*,[172] has been synthesized in eight steps (21—23 % overall yield).[173] A synthesis of mimosamycin (185), which was isolated from a species of *Reniera*,[174] has been reported.[175] In addition to the usual dibromotyrosine-derived metabolites found in *Aplysina aerophoba*, a Canary Islands specimen contained aplysinadiene (186) and the oxazolidinone (187).[176] The structure of aplysinadiene (186) was elucidated by interpretation of spectral data and confirmed by synthesis, while the structure of the oxazolidinone (187), which appears to be a diastereoisomer of compounds reported previously,[177,178] was determined by *X*-ray analysis.

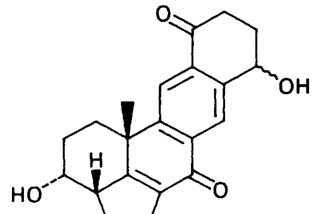
A Red Sea species of *Smenospongia* contains the known prenylated quinone ilimaquinone (188)[179] and a new cytotoxic and antimicrobial aminoquinone called smenospongine (189).[180] A specimen of *Hippospongia* cf. *metachromia* from Okinawa has provided two new prenylated quinones, namely metachromins A (190) and B (191), in addition to the known



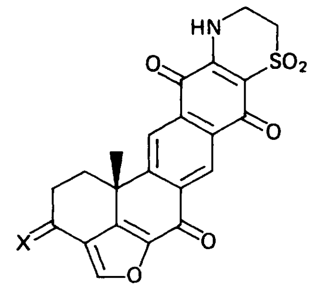
(192) X = H_2
(193) X = O



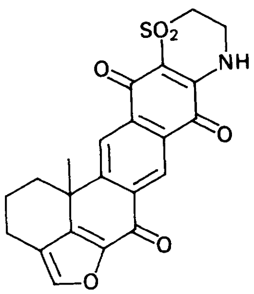
(194)



(195)



(196) X = H_2
(198) X = O



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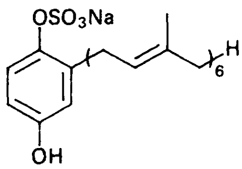

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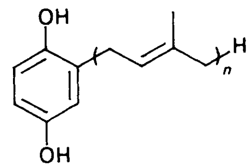
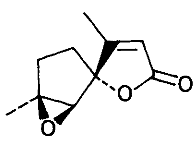
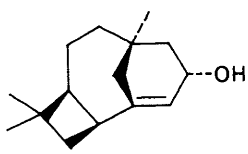


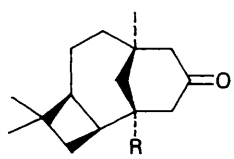
(200) n = 7
(201) n = 8



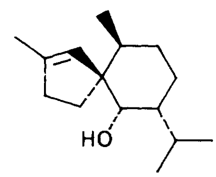
(202)



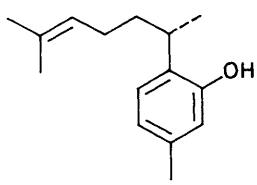
(203)



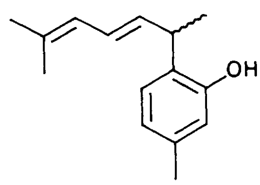
(204) R = OH
(205) R = OMe



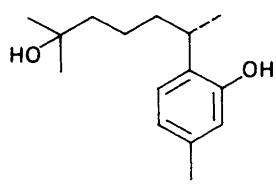
(206)



(207)



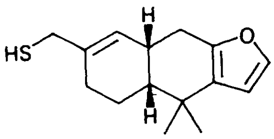
(208)



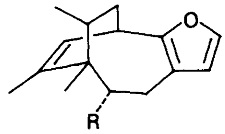
(209)

compound isospongiaquinone.[181] The metachromins, which were identified by spectroscopic analysis, exhibited *in vitro* activity against L1210 leukaemia cells and showed potent coronary vasodilating activity. The known metabolites xestoquinone (192)[182] and halenaquinone (193)[183] were isolated from a species of *Adocia* from Truk, together with five new minor metabolites (194)—(198).[184] The most interesting of the new metabolites are adociaquinone A (196) and the mildly cytotoxic adociaquinone B (197), which were synthesized by reacting xestoquinone (192) with hypotaurine (a common though rarely reported metabolite of sponges), and 3-ketoadociaquinone (198), which was synthesized in like manner from halenaquinone. A total synthesis of halenaquinone (193) and the corresponding hydroquinone from the optically active Wieland–Miescher ketone has provided the absolute configurations of the natural products.[185] Hexaprenylhydroquinone sulphate (199) was identified as an H, K-ATPase inhibitor from a Japanese species of *Dysidea*.[186] Both heptaprenylhydroquinone (200) and octaprenylhydroquinone (201) were isolated from a Tunisian specimen of *Hippospongia communis*.[187]

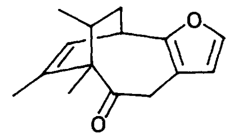
The first monoterpenoid to be isolated from a sponge is adriadysiolide (202), which was isolated from a North Adriatic species of *Dysidea*.[188] The structure proposed for adriadysiolide (202) was confirmed by a stereorational total synthesis. A New Zealand species of *Eurypon* contains four new sesquiterpenes, three of which (203)–(205) possess the carbon skeleton of β-caryophyllene alcohol while the fourth (206) has the axane skeleton.[189] The structures of (203)—(206) were deduced by interpretation of spectroscopic data. The alcohol (204) and corresponding methyl ether (205) are thought to be artefacts of the isolation procedure. A Japanese species of *Epipolasis* contained the sesquiterpenoids (+)-curcuphenol (207), dehydrocurcuphenol (208), and the related alcohol (209).[190]



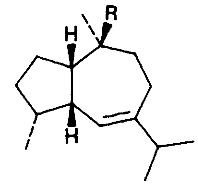
(210)



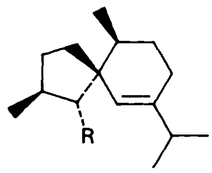
(211) R = OAc
(212) R = OH



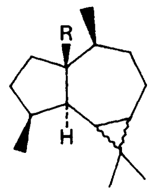
(213)



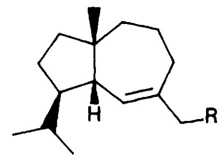
(214) R = NC
(215) R = NCS
(216) R = NHCHO



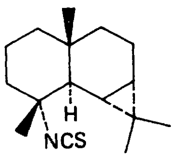
(217) R = NC
(218) R = NCS



(219) R = NC
(220) R = NCS



(221) R = NC
(222) R = NCS



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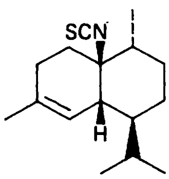

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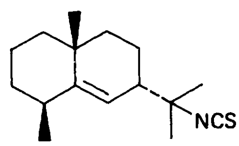

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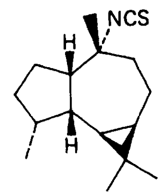

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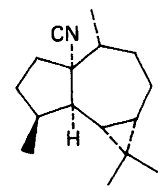

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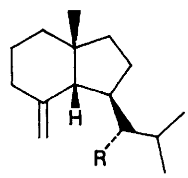
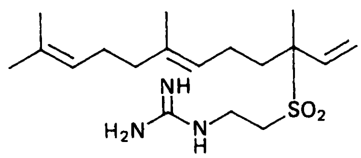
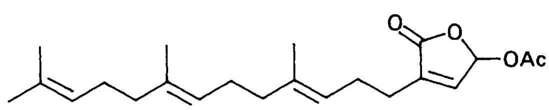


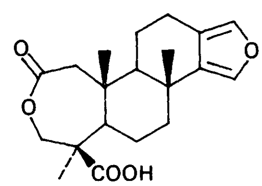
(228) R = NC
(229) R = NHCHO



(230)



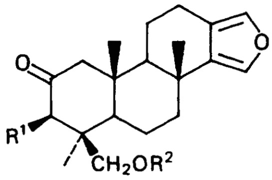
(231)



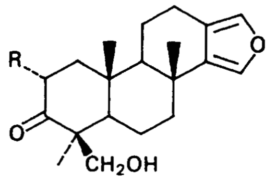
(232)

The curcuphenols (207) and (208) showed strong inhibitory activity against H,K-ATPase. The isolation of thiofurodysinin (210) from an Australian specimen of *Dysidea avara* represents the first report of a sesquiterpene mercaptan from a sponge.[191] 5-Acetoxynakafuran 8 (211), 5-hydroxynakafuran 8 (212) and 5-ketonakafuran 8 (213) have been isolated from *Dysidea etheria* from Bermuda.[192] A report of a new isonitrile (214), isothiocyanate (215), and formamide (216) trio based on the guai-6-ene skeleton from an unidentified sponge provided some evidence that the formamide might be an artefact of isolation.[193] Three new isonitrile-isothiocyanate pairs (217)—(222) have been found as minor metabolites of *Acanthella acuta*.[194] The structures of (217)—(222) were elucidated by interpretation of spectral data. The related sponge *A. pulcherrima* from Australia has yielded two new isothiocyanates (223) and (224) in addition to the known sesquiterpenes (225)—(227).[195] The syntheses of axisonitrile-1 (228) and axamide-1 (229), which are metabolites of *Axinella cannabina*,[196—198] and the corresponding 10-*epi*-derivatives have been reported.[199] A simple synthesis of agelasidine A (230) from a species of *Agelas*[200] employs a hetero-Claisen rearrangement.[201]

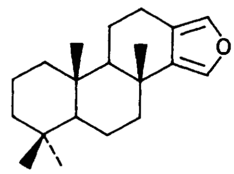
Dictyodendrillolide (231) is a prenylated butenolide from a rare species of *Dictyodendrilla* from the Great Barrier Reef.[202] *Spongia arabica* from the Red Sea contains a new spongian derivative called spongialactone A (232).[203] A specimen of *Hyatella intestinalis* contained three novel spongian diterpenes



(233) R^1 = OAc, R^2 = H
(236) R^1 = OH, R^2 = H
(237) R^1 = OAc, R^2 = Ac



(234) R = H
(235) R = OH



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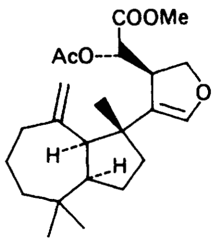

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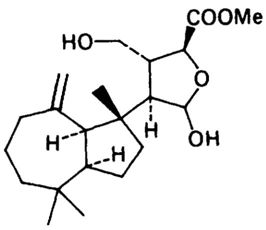

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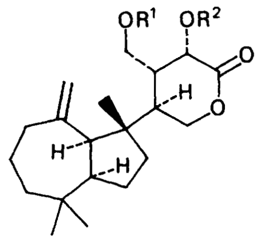
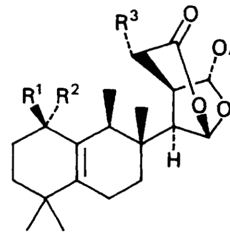
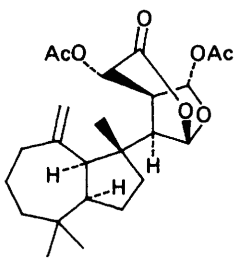


(241) R^1 = R^2 = Ac
(242) R^1 = Ac, R^2 = H
(243) R^1 = R^2 = H



(244) R^1 = R^2 = R^3 = H
(245) R^1 = R^3 = H, R^2 = OH
(247) R^1 = OH, R^2 = R^3 = H
(248) R^1 = R^2 = H, R^3 = OAc
(249) R^1 = OH, R^2 = H, R^3 = OAc



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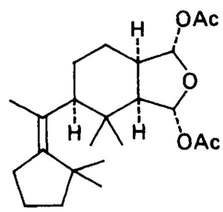

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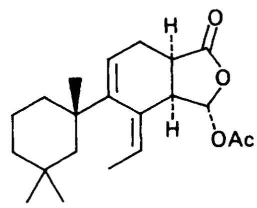

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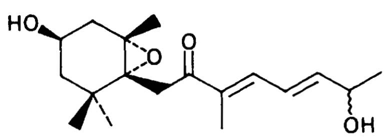

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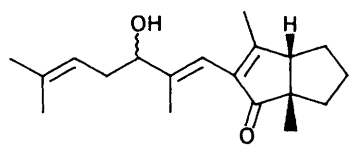

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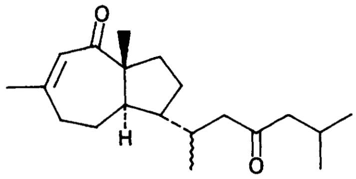
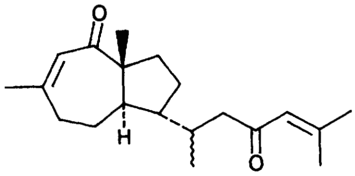
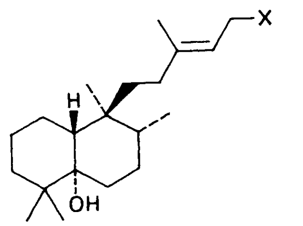


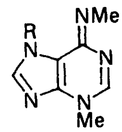
(254)

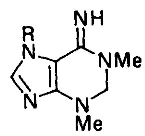


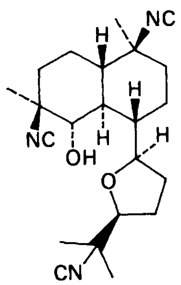
(255)

(233), (234), and (235), together with the known compounds (236)—(238) that had previously[204,205] been isolated from various species of *Spongia*.[206] Ten new rearranged spongian diterpenes have been isolated from two Red Sea species of *Dysidea*.[207] One species of *Dysidea* contained shahamins A—G (239)—(245), in addition to the known diterpene macfarlandin E (246).[208] The second *Dysidea* species contained shahamins F (244), H (247), I (248), and J (249). The structures of the shahamins were proposed on the basis of their spectral data supported by chemical interconversions.[207] Two new nor-diterpenes (250) and (251) have been isolated as minor constituents of *Spongionella gracilis*.[209] The nor-diterpene (250) has an unprecedented carbon skeleton. The apocarotenoid xestodiol (252)[210] and the novel nor-diterpene xestenone (253)[211] are metabolites of *Xestospongia vanilla* that were identified from their spectral properties. Reiswigins A (254) and B (255) are antiviral diterpenes from the deep-water sponge *Epipolasis*



(256) X = 

(257) X = 



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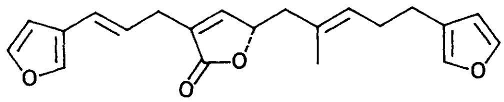

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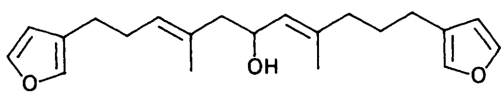

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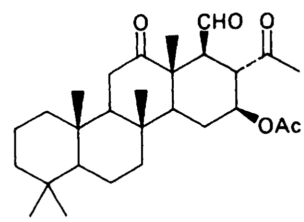

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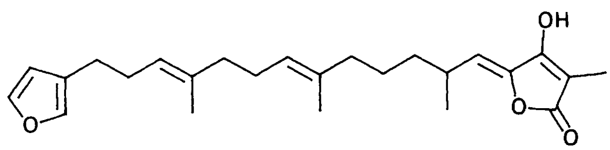

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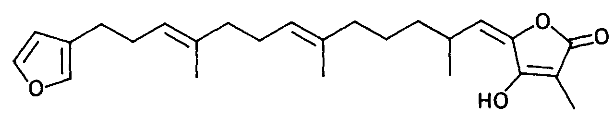

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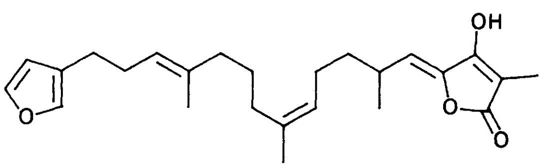

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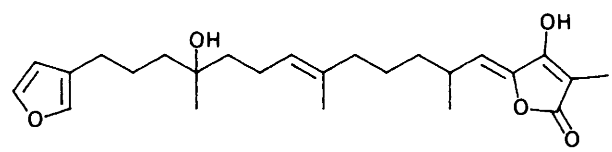

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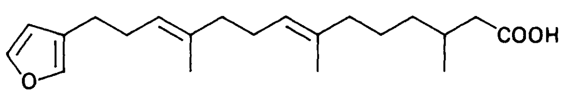
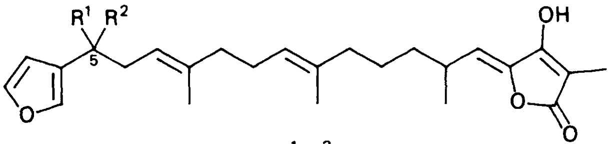


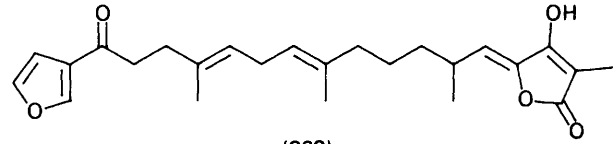
(266)

reiswigi.[212] The structural elucidation by interpretation of spectral data is very sparsely outlined. Two diterpene alkaloids, agelasimine-A (256) and agelasimine-B (257), were obtained from *Agelas mauritiana* from Enewetak Atoll.[213] The stereochemistry of the diterpene portion of the agelasimines had been determined previously by *X*-ray analysis of a derivative.[214] The agelasimines (256) and (257) are cytotoxic and may act as calcium channel antagonists and a_1 adrenergic blockers. One additional diterpene isonitrile, isokalihinol F (258), was obtained from a Fijian specimen of *Acanthella cavernosa*.[215]

The absolute configuration of kurospongin (259), which is a novel fish-feeding inhibitor from an Okinawan specimen of *Spongia*, was determined by application of the Horeau method to the diol formed by reaction of (259) with ethyl magnesium bromide.[216] *Carteriospongia flabellifera* from the Great Barrier Reef was reported to contain 12,13-didehydrofurospongin-1 (260) and the homosesterterpene (261), both of which were identified from spectral properties.[217] The complete stereochemistry of variabilin (262), which was originally isolated from *Ircinia variabilis*,[218] has recently been defined. Both variabilin (262) and the corresponding 20*E* isomer (263) were isolated from a species of *Sarcotragus*, that also contained the sesterterpenes (264) and (265) and the C_{21} furanoterpene (266).[219] A New Zealand species of *Ircinia* produces variabilin (262), the alcohol (265), and a series of four sesterterpenes



(267) R¹,R² = O
(268) R¹ = OH, R² = H



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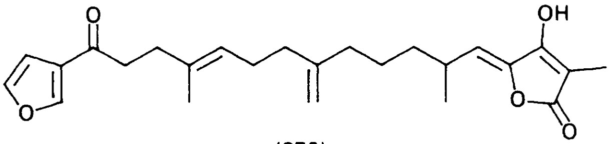

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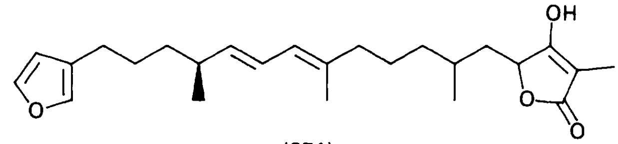

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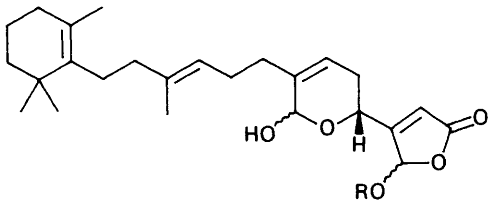
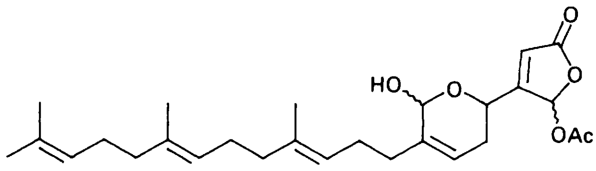


(272) R = Ac
(275) R = H



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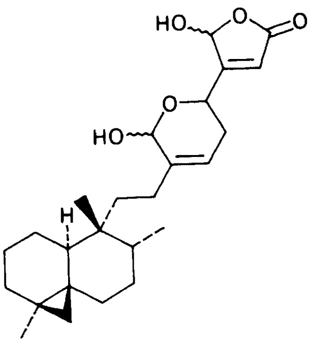

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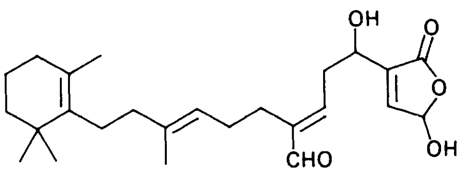

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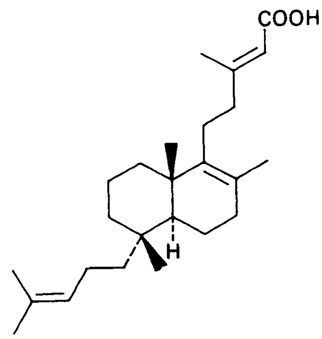
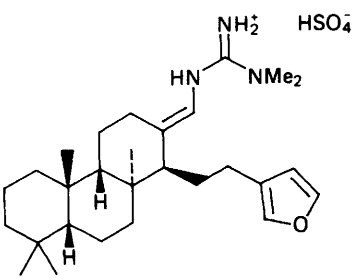
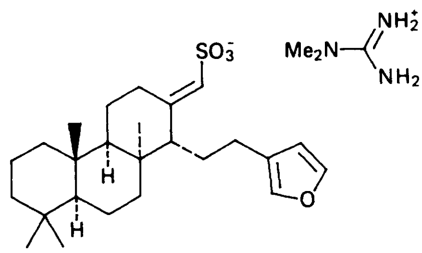


(277)

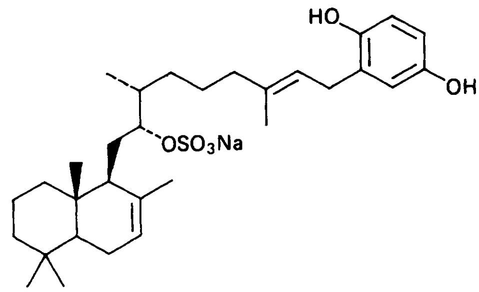


(278)

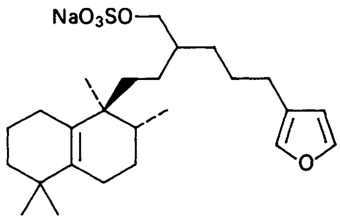


(279)

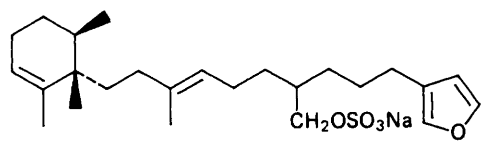
(267)—(270) that are oxygenated at C-5.[220] An Australian species of *Ircinia* contains the antibacterial sesterterpene (271), the structure of which was elucidated by analysis of spectral data and chemical degradation.[221] Manoalide 25-monoacetate (272) and the corresponding 'linear' isomer, thorectolide monoacetate (273), were isolated from two different specimens of *Thorectandra excavatus*, while other specimens contained mixtures of the two compounds.[222] Cacospongionolide (274) is an unusual cytotoxic sesterterpene from a specimen of *Cacospongia mollior* from the Tyrrhenian Sea.[223] The structure of cacospongionolide (274), which belongs to a new skeletal class, was elucidated by interpretation of spectral data. The absolute configuration of manoalide (275), which is an anti-inflammatory agent from *Luffariella variabilis*,[224] has been determined by total synthesis of a derivative from 2-deoxy-D-ribose.[225] An additional synthesis of manoalide (275), which involves the intermediacy of seco-manoalide (276), has been outlined.[226] The total synthesis of dysideapalaunic acid (277), which is an unreported(!) aldose reductase inhibitor from a Palauan species of *Dysidea*, has established the absolute configuration.[227] The structure of suvanine, which is an acetyl cholinesterase inhibitor from a species of *Coscinoderma* found in both Fiji and Palau, has been revised from (278)[228] to (279).[229] A Californian sponge of the family Halichondriidae



(280)



(281)



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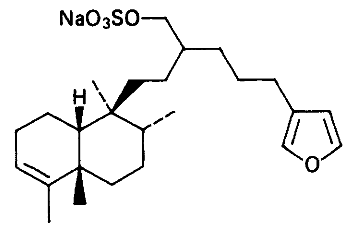

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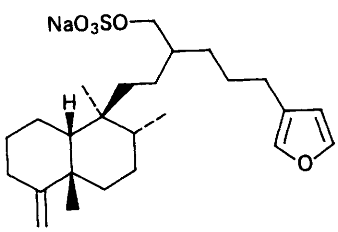
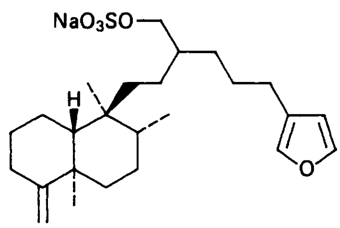


(284)



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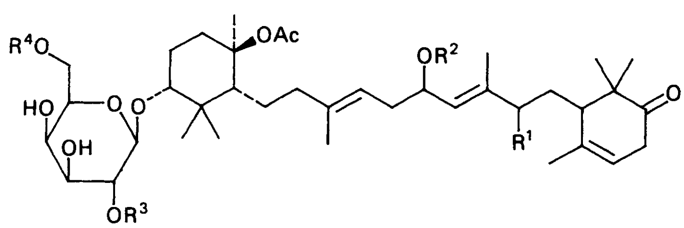
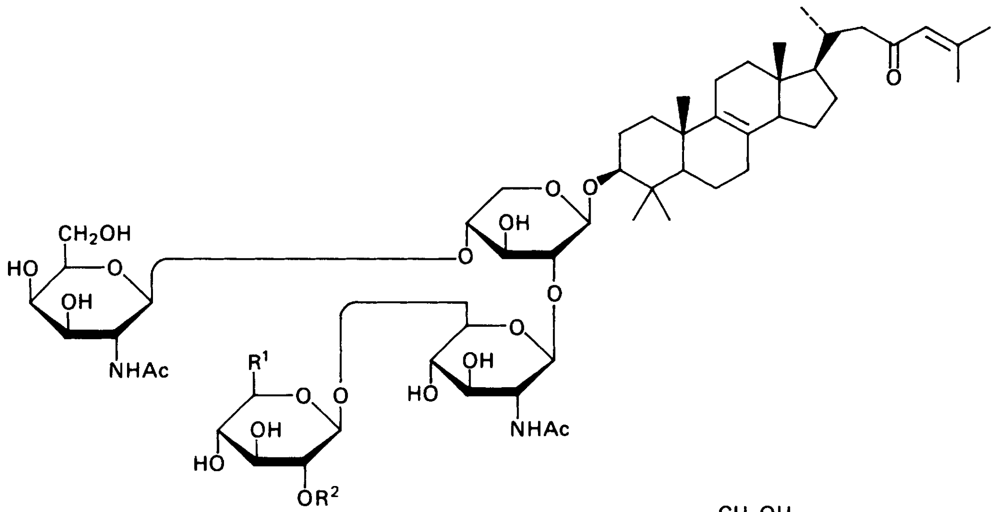


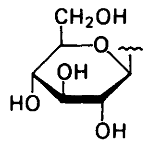
(286) R^1 = OAc, R^2 = Ac, $R^3 = R^4$ = H
(287) R^1 = OAc, $R^2 = R^3 = R^4$ = H
(288) $R^1 = R^3 = R^4$ = H, R^2 = Ac
(289) R^1 = OAc, $R^2 = R^3$ = Ac, R^4 = H
(290) R^1 = OAc, $R^2 = R^4$ = Ac, R^3 = H

contained the sulphated sesterterpene hydroquinone (280) and five sulphated sesterterpenes (281)—(285).[230] The structures of halisulphates 1—5 (280)—(284) were determined by interpretation of spectral data and the structure (285) was proposed for halisulphate 6. The halisulphates possess antimicrobial and anti-inflammatory properties.

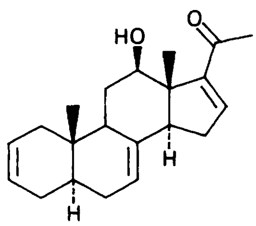
Pouosides A—E (286)—(290) are triterpene galactosides from a Trukese species of *Asteropus*.[231] The novel carbon skeleton of the pouosides was identified by interpretation of spectral data. The same sponge also contained sarasinoside A_1 (291).[232] Sarasinosides A_1 (291), B_1 (292), and C_1 (293) are ichthyotoxic and cytotoxic constituents of *Asteropus sarasinosum* from Palau.[233] The structure of the sapogenol was determined by *X*-ray analysis and the structures of the natural



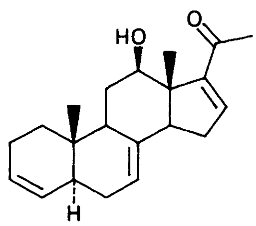
(291) $R^1 = CH_2OH$, R^2 = a
(292) R^1 = H, R^2 = a
(293) R^1 = H, R^2 = H



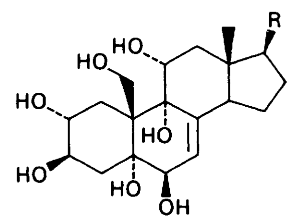
= a



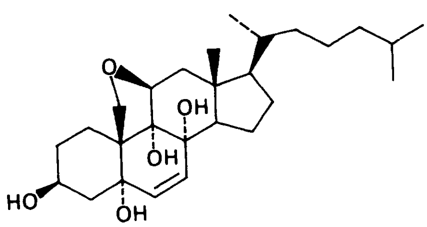
(294)



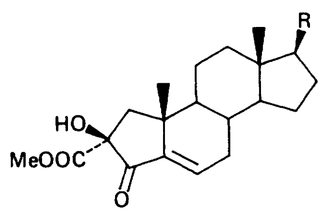
(295)

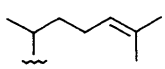


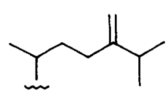
(296)

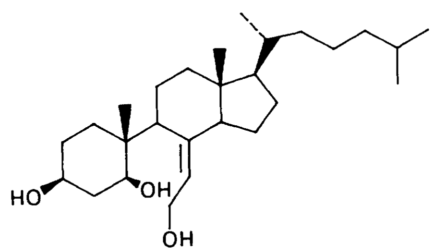


(297)

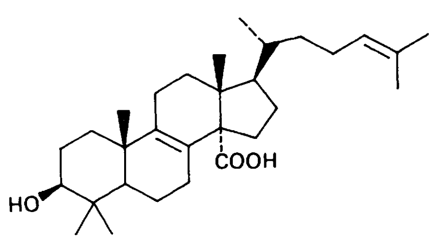


(298) R = 

(299) R = 

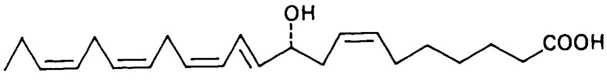


(300)

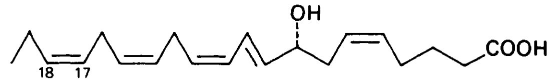


(301)

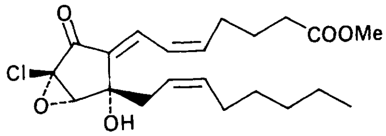
products were elucidated by analysis of spectral data. Two unusual steroids, agnatasterones A (294) and B (295), were isolated from *Axinella agnata*.[234] Eight new polyhydroxylated sterols based on the 5α-cholest-7-ene-2α,3β,5α,6β,9α,11α,19-heptol nucleus (296) were found in *Dysidea etheria*.[235] A related sterol, 11β,19-epoxycholest-6-en-3β,5α,8α,9α-tetrol (297) is produced by *Dysidea tupha*.[236] The ring A contracted sterols, anthosterones A (298) and B (299), were obtained from *Anthoracuata graceae*.[237] The structure of hipposterol (300), which is a 5,6-secosterol from *Hippospongia communis*, was confirmed by synthesis.[238] Penasterol (301) is a novel triterpene from an Okinawan species of *Penares*, that shows potent antileukemic activity.[239]



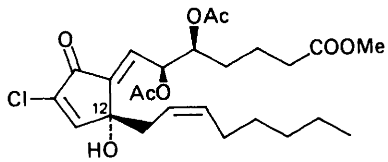
(302)



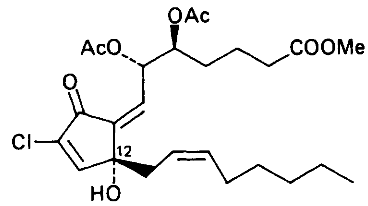
(303)
(304) 17,18-dihydro



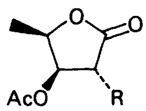
(305)



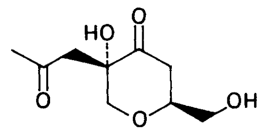
(306)



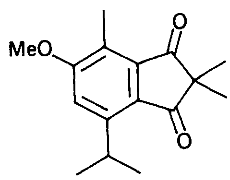
(307)



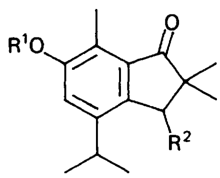
(308) R = $C_{16}H_{33}$
(309) R = $C_{14}H_{29}$



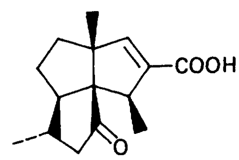
(310)



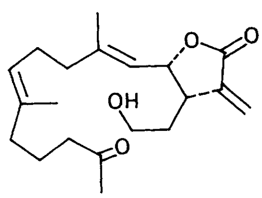
(311)



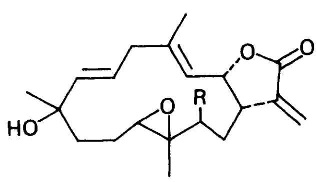
(312) R^1 = Me, R^2 = OH
(313) R^1 = Me, R^2 = OAc
(314) R^1 = H, R^2 = H
(315) R^1 = Me, R^2 = H



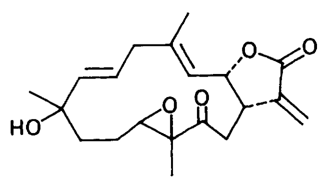
(316)



(317)



(318) R = H
(319) R = OAc



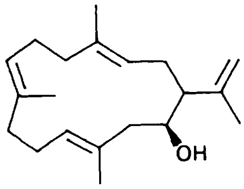
(320)

8 Coelenterates

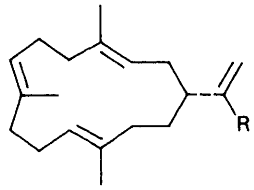
In a departure from previous reviews in this series, the metabolites of coelenterates are grouped by chemical class rather than phylogenetically by Order. The prostanoids and other eicosanoids from coelenterates continue to evoke interest. Leiopathic acid (302) and two known eicosanoids, (303) and (304), were isolated from a black coral, *Leiopathes* sp., collected at St Paul Island in the South India Ocean.[240] A new epoxyprostanoid (305) which has antiproliferative properties was isolated as a minor metabolite of the Japanese stoloniferan coral *Clavularia viridis*.[241] Total synthesis of several possible isomers has allowed the structures of (7*E*)- and (7*Z*)-punagladin 4 to be revised to (306) and (307) respectively from the corresponding 12*S* epimers.[242] A second synthesis of punaglandin 4 (306) involved the enzymic resolution of the key chlorocyclopentene intermediate.[243] The absolute configurations of the lactones (308) and (309) from the gorgonian *Plexaura flava*[244] were determined by synthesis of their optical enantiomers from (*S*)-lactic acid.[245] The (*S*,*S*) configuration of (−)-bissetone (310), which is a metabolite of *Briareum polyanthes*,[246] has been established by total synthesis from D-glucose.[247]

An unnamed soft coral of the genus *Primnoeides* is the source of a family of five sesquiterpenes (311)—(315) that contain a new carbon skeleton.[248] The structure of the alcohol 3-hydroxy-6-methoxyprimnatrienone (312) was determined by *X*-ray analysis and the remaining primnatriene derivatives were identified by comparison of spectral data. Subergorgic acid (316), which is a cardiotoxic sesquiterpene from the gorgonian *Subergorgia suberosa*,[249] has been synthesized by a stereoselective route.[250]

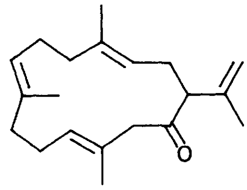
Mayolide A (317) is a novel secocembranoid that was isolated from the soft coral *Sinularia mayi* together with the cembranoid lactones mayolides B (318), C (319), and D (320).[251] The



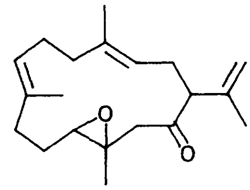
(321)



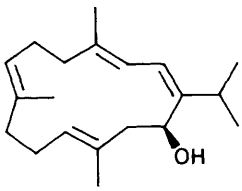
(322) R = CH_2OH
(323) R = CHO
(324) R = COOH



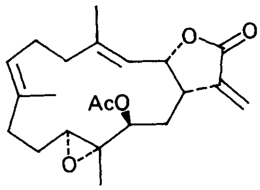
(325)



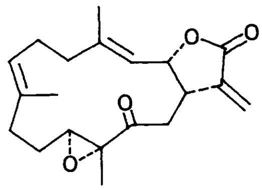
(326)



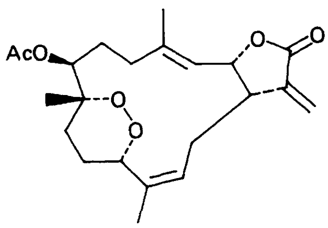
(327)



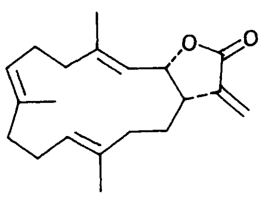
(328)



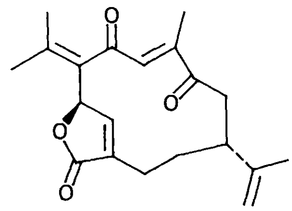
(329)



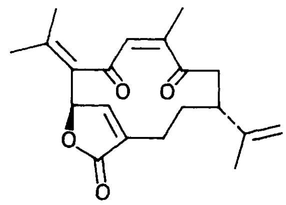
(330)



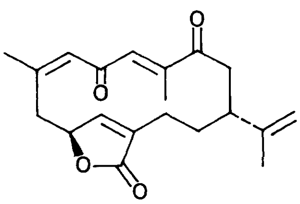
(331)



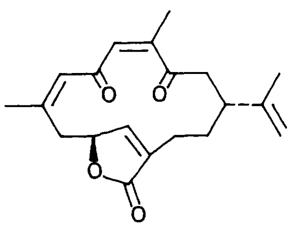
(332)



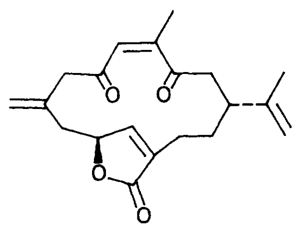
(333)



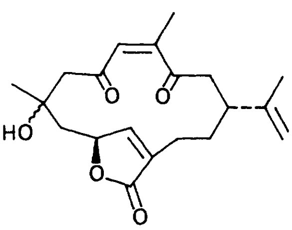
(334)



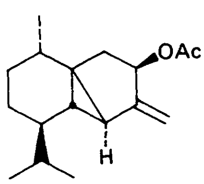
(335)



(336)



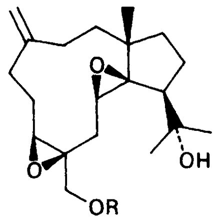
(337)



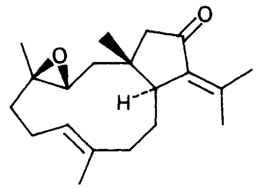
(338)

structures of the mayolides were elucidated by interpretation of spectral data and interconversion with known compounds. It has been suggested that some of the six minor cembranoids (321)—(326) isolated from *S. mayi* might be plausible precursors of the major cembranolides found in the soft coral. The structures of sinulariols C (321) and D (322), sinularial A (323), sinularic acid (324), and sinularones A (325) and B (326) were elucidated by physicochemical methods.[252] The oxidation chemistry of sarcophytol A (327), which is a potent anti-tumour-promoter from *Sarcophyton glaucum*, has been reported.[253] Three known cytotoxic cembranolides were isolated from *Sinularia mayi*: the stereochemistry of cembranolides (328) and (329), previously reported from *Lobophytum pauciflorum*,[254,255] were determined by *X*-ray crystallography and spectral methods, respectively, and the absolute configuration of denticulatolide (330), which is a metabolite of *L. denticulatum*,[256] was determined by *X*-ray analysis of a *p*-bromobenzoate derivative.[257] The cembranolide (331), which is a metabolite of the soft coral *Lobophytum michelae*,[258] has been synthesized.[259] The strategies employed in the synthesis of cembranes and cembranolides have been reviewed in detail.[260]

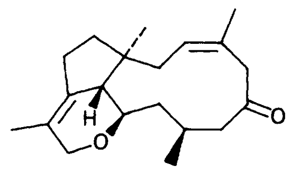
The minor metabolites of both Atlantic and Pacific specimens of *Gersemia rubiformis* have been compared.[261] The Pacific coast animals yielded two new pseudopterane diterpenoids, isogersemolides A (332) and B (333), and four new cembranoids: isoepilophodiones A (334), B (335), and C (336) and rubifol (337). The Atlantic coast animals contained 3-acetoxy-β-cubebene (338). The proposed structures are all based on spectroscopic analysis and chemical interconversion. The cytotoxic activity of a Japanese species of *Clavularia* is due



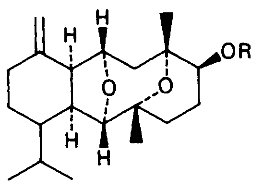
(339) R = H
(340) R = Ac



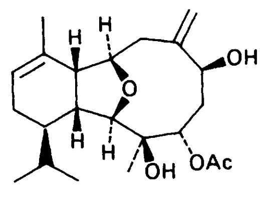
(341)



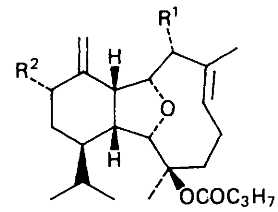
(342)



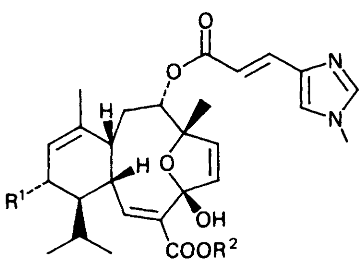
(343) R = H
(344) R = Ac



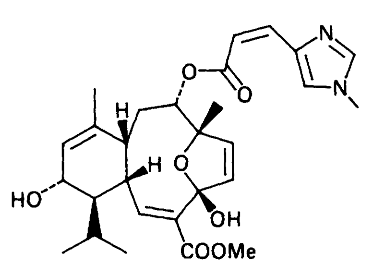
(345)



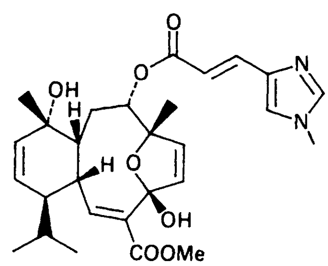
(346) $R^1 = R^2 = H$
(347) $R^1 = OCOC_3H_7$, $R^2 = H$
(348) $R^1 = H$, $R^2 = OH$



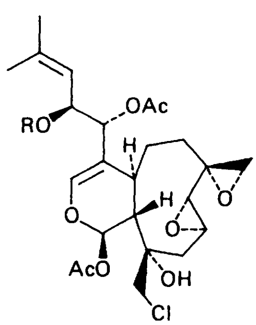
(349) $R^1 = H$, $R^2 = Me$
(350) $R^1 = H$, $R^2 = Et$
(351) $R^1 = OH$, $R^2 = Me$
(352) $R^1 = OAc$, $R^2 = Me$



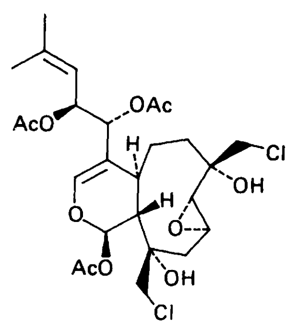
(353)



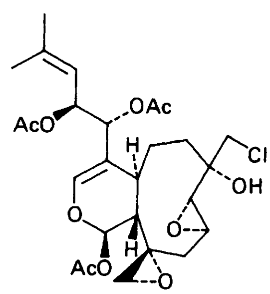
(354)



(355) R = Ac
(358) R = H



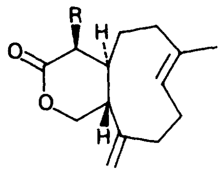
(356)



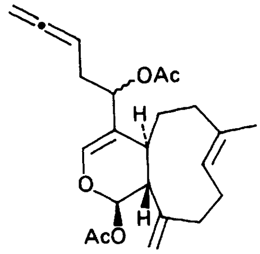
(357)

to stolonidiol (339), the acetate (340) and claenone (341), the structures of which were determined on the basis of spectroscopic data and the *X*-ray analysis of a derivative.[262,263] A related diterpene (342) has been reported from a Chinese species of *Clavularia*.[264] Sclerophytins A (343) and B (344) are two cytotoxic diterpenes from the soft coral *Sclerophytum capitalis* from Enewetak that were identified by interpretation of spectral data.[265] A new cladiellane diterpene called alcyonin (345) was isolated from *Sinularia flexibilis* and identified by using spectroscopic and chemical methods.[266] Three similar diterpenes, litophynins A (346), B (347), and C (348), that inhibit insect growth in the silkworm *Bombyx mori*, were isolated from a Japanese species of *Litophyton*.[267,268] The structures and absolute configuration of the litophynins were established on the basis of spectral and chemical evidence. The Mediterranean stolonifer *Sarcodictyon roseum* contains six novel diterpenoids that are esterified by *N*-methylurocanic acid.[269,270] The structures of sarcodictyins A (349), B (350), C (351), D (352), E (353), and F (354) were elucidated by spectroscopic methods and the absolute configurations were determined by Horeau's method.

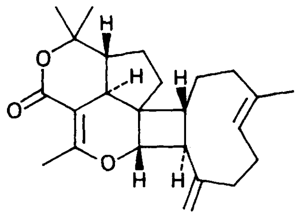
Four new xenicane diterpenes – havannachlorhydrine-11(19) (355), havannadichlorhydrine-7(18), 11(19), (356), havannachlorhydrine-7(18) (357), and 13-desacetylhavannachlorhydrine-11(19) (358) – were isolated from *Xenia membranacea* and their structures were determined by correlation with a derivative



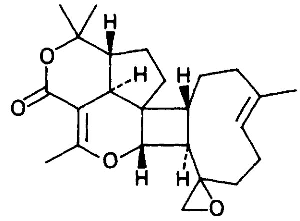
(359) R = $-(CH_2)_3CH{=}CH_2$
(360) R = $-(CH_2)_2CH{=}C{=}CH_2$



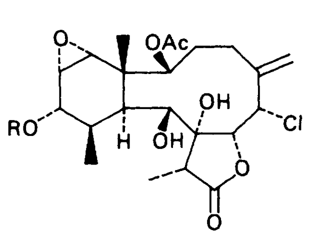
(361)



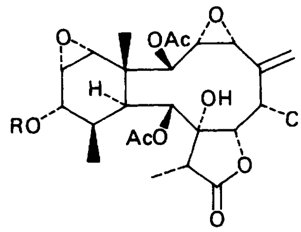
(362)



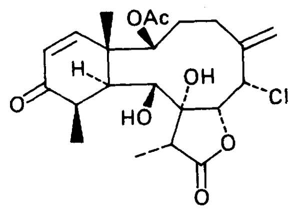
(363)



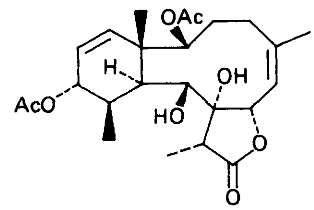
(364) R = COC_5H_{11}
(365) R = Ac



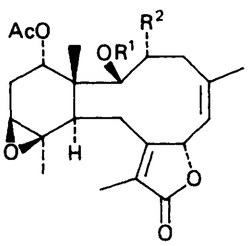
(366) R = H
(367) R = Ac



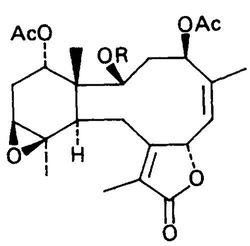
(368)



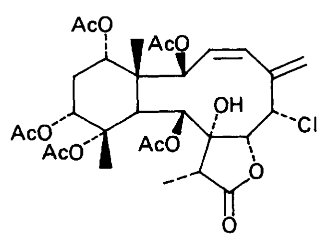
(369)



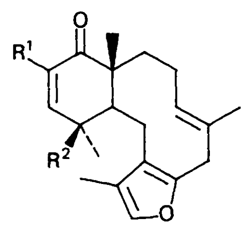
(370) $R^1 = COC_3H_7$, R^2 = OAc
(371) $R^1 = COC_3H_7$, R^2 = H



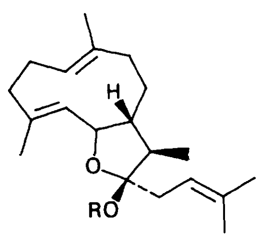
(372) R = COC_3H_7
(373) R = COC_2H_5



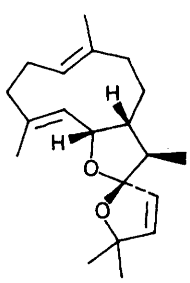
(374)



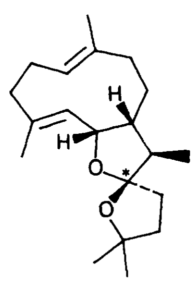
(375) $R^1 = R^2$ = H
(376) R^1 = H, R^2 = OH
(377) R^1 = Cl, R^2 = OH



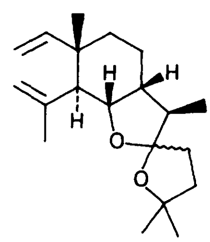
(378) R = H
(380) R = Me



(379)



(381)
(382) (epimer at *)

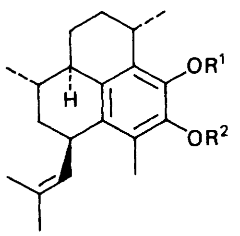


(383)

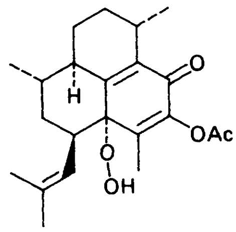
that was subjected to *X*-ray analysis.[271] Acalycixeniolides A (359) and B (360) are cytotoxic norditerpenes of the xenicane type that were isolated from *Acalycigorgia inermis* and identified by spectroscopic studies.[272] A related allene, ginamallene (361), was isolated from four Japanese species of *Acalycigorgia*.[273] Two novel C_{24} 'acetoacetylated' diterpenes, antheniolides A (362) and B (363), were obtained from *Anthelia glauca*.[274] The structures of the antheniolides were established by using spectroscopic methods and a biosynthetic route from xeniaphyllane[275] is proposed.

An Indopacific gorgonian of the genus *Solenopodium* contains six new diterpenes of the briarane class.[276] The structures of solenolides A—F (364)—(369) were assigned on the basis of spectral analyses and chemical modifications. Solenolides A (364), D (367), and E (368) are antiviral and anti-inflammatory agents while solenolide F (369) shows only anti-inflammatory activity. Four new briaranes (370)—(373) have been isolated from *Briareum steckei*.[277] The structures of (372) and (373) were determined by *X*-ray analyses and the major metabolites (370) and (371) were identified by spectroscopic means. Brianthein V (374) is a new cytotoxic and antiviral diterpene from *Briareum asbestinum*.[278] The relatively simple briaranes, verecynarmins B (375), C (376), and D (377), that were found in both the sea pen *Veretillum cynomorium* and the nudibranch mollusc *Armina maculata*, all undergo very slow conformational interconversion in solution.[279] The structures of the verecynarmins were deduced by interpretation of their complex spectral data and by chemical modification.

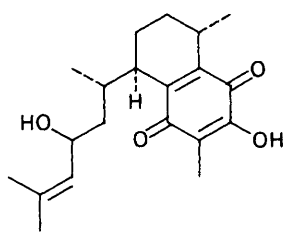
Asperketals A—F (378)—(383) are new diterpenes of the dilophol class from the gorgonian *Eunicea asperula*, the



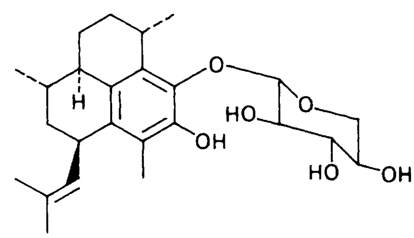
(384) R^1 = Ac, R^2 = H
(385) R^1 = H, R^2 = Ac



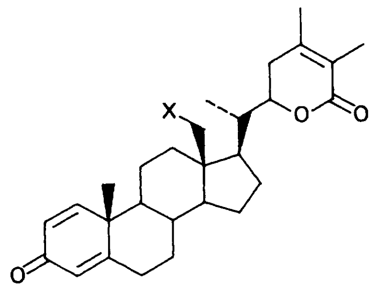
(386)



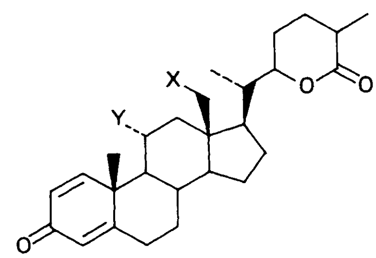
(387)



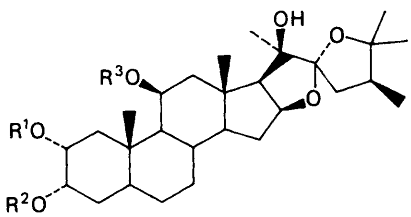
(388)



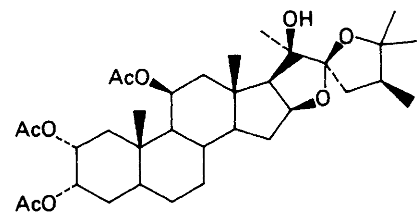
(389) X = H
(390) X = OAc
(391) X = H (1,2-dihydro)



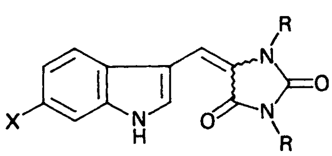
(392) X = Y = H
(393) X = OAc, Y = H
(394) X = H, Y = H (1,2-dihydro)
(395) X = OAc, Y = H (1,2-dihydro)
(396) X = H, Y = OAc (1,2-dihydro)



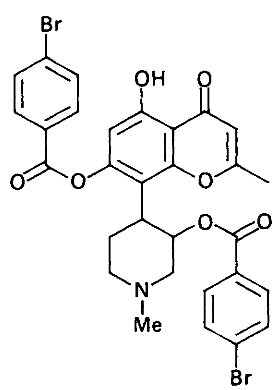
(397) $R^1 = R^2 = R^3$ = Ac
(398) $R^1 = R^2$ = Ac, R^3 = H
(399) $R^1 = R^3$ = H, R^2 = Ac
(400) $R^1 = R^2 = R^3$ = H



(401)



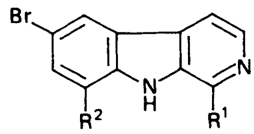
(402) R = Me, X = H
(403) R = Me, X = Br
(404) R = H, X = H
(405) R = H, X = Br



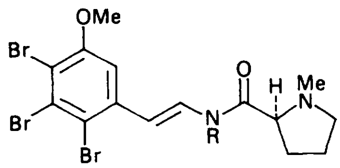
(406)

structures of which were assigned on the basis of chemical and spectroscopic studies.[280] A Caribbean gorgonian of the genus *Pseudopterogorgia* contains three new pseudopterosins (384)—(386) and one new seco-pseudopterosin (387) that were identified by spectral and chemical experiments.[281] A mechanism linking the two series of compounds through the hydroperoxide (386) is described. (−)-Pseudopterosin A (388), which is an anti-inflammatory diterpene from the gorgonian *Pseudopterogorgia elizabethae*,[282] has been synthesized from (−)-limonene.[283] Eight new steroidal lactones (389)—(396) of the withanolide class have been isolated from a Trukese species of *Minabea*[284] and five new hippurins (397)—(401) were obtained from an Indian specimen of *Isis hippuris*.[285]

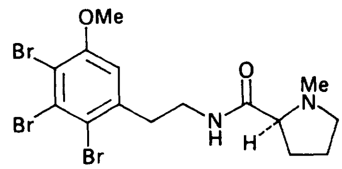
A scleractinian coral of the genus *Tubastrea* from the Philippines has yielded two new aplysinopsin derivatives, (402) and (403), each of which occurred as a 5:2 mixture of *E* and *Z* stereoisomers.[286] Two similar compounds (404) and (405) were isolated as 1:1 mixtures of stereoisomers from *Leptopsammia pruvoti* from the Mediterranean.[286] The structures of the new aplysinopsin derivatives were derived by interpretation of spectral data and confirmed by synthesis. The *E*/*Z* isomerization is a photochemical rearrangement. Tubastraine (406) is a novel alkaloid from the stony coral *Tubastrea micrantha* that was isolated along with heteronemin, which is a well-known sponge metabolite[287] and most likely a contaminant.[288] Tubastraine looks suspiciously like the bis-*p*-bromobenzoate of the terrestrial alkaloid rohitukine. The



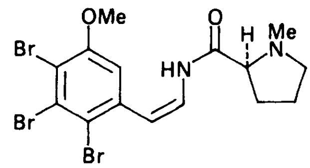
(407) R^1 = Et, R^2 = H
(408) R^1 = Me, R^2 = H
(409) R^1 = Et, R^2 = Br



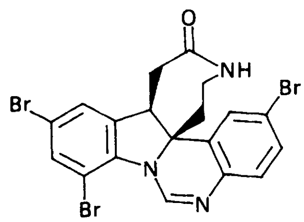
(410) R = Me
(412) R = H



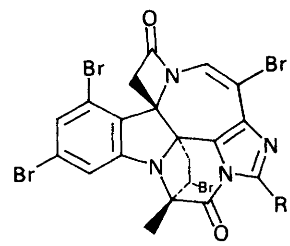
(411)



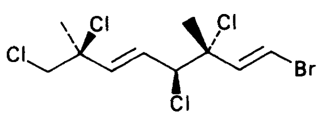
(413)



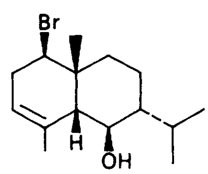
(414)



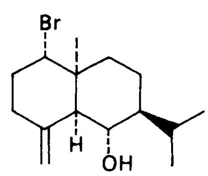
(415) R = H
(416) R = Br



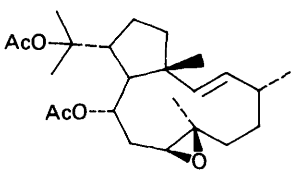
(417)



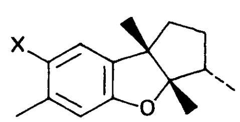
(418)



(419)



(420)



(421) X = Br
(422) X = H

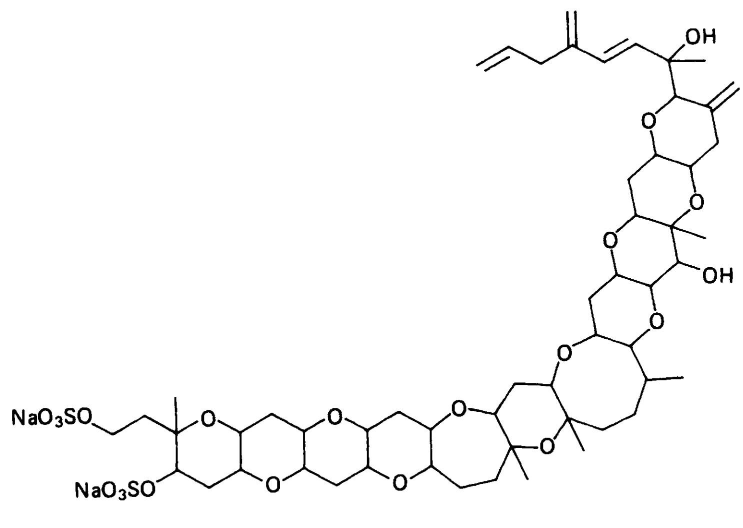
hydroid *Aglaophenia pluma* contains three alkaloids, (407), (408), and (409), that are reminiscent of the β-carbolines found in tunicates.[289] The structures of (407)—(409) were deduced from spectral data and confirmed by synthesis.

9 Bryozoans

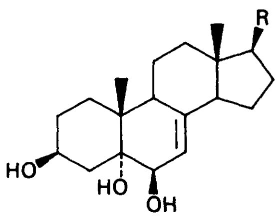
Chemical studies of bryozoans are clearly limited by collection constraints and few new results have been reported. Four new bromine-containing alkaloids, amanthamides C—F (410)—(413), have been isolated from various collections of *Amathia wilsoni* from Tasmania.[290] The ratios of the amanthamides, which were identified by spectral analysis, vary according to the collection site. The structure of hinckdentine-A (414), which is a novel alkaloid from the Tasmanian bryozoan *Hinksinoflustra denticulata*, was determined by *X*-ray analysis.[291] Chartellamides A (415) and B (416) are the latest β-lactams to be isolated as minor constituents of *Chartella papyracea*.[292] The structures of the chartellamides were deduced by interpretation of spectral data.

10 Molluscs

The metabolites isolated from sea hares are invariably obtained from an algal dietary source. Aplysiaterpenoids A (81) and B (417) are two new halogenated monoterpenes from *Aplysia kurodai*.[293] Aplysiaterpenoid A (81) has been reported as a major metabolite of *Plocamium hamatum*[91] and (417) is closely related to a known algal metabolite from a species of *Plocamium*.[294] The structures of the aplysiaterpenoids were determined by *X*-ray analyses. The eudesmane sesquiterpenes, lankalapuols A (418) and B (419), that were isolated from a Sri Lankan specimen of *Aplysia dactylomela* are closely related to certain *Laurencia* (red alga) metabolites. The structures of the lankalapuols, which are antipodal, were based on spectral studies and the structure and absolute configuration of lankalapuol A (418) was determined by an *X*-ray analysis performed on the corresponding acetate.[295] A Canary Islands specimen of *A. dactylomela* contained a dolabellane epoxide (420) that is a typical constituent of brown algae.[296] A stereocontrolled synthesis of aplysin (421) and debromoaplysin (422), which are metabolites of *Aplysia kurodai*, involves the ring expansion of a cyclobutane intermediate.[297]



(423)



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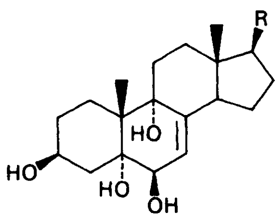

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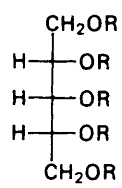

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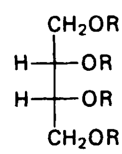

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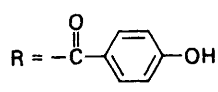
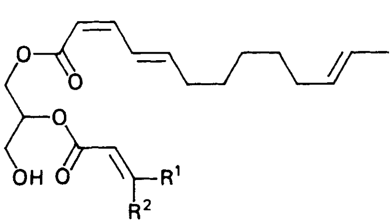
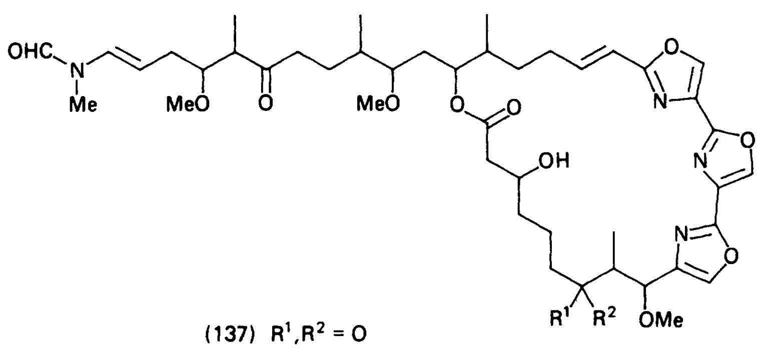




(428) $R^1 = R^2 = Me$

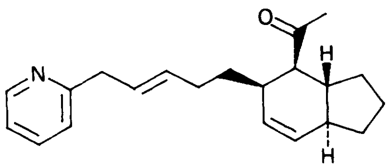
(429) $R^1 = SMe$, $R^2 = H$



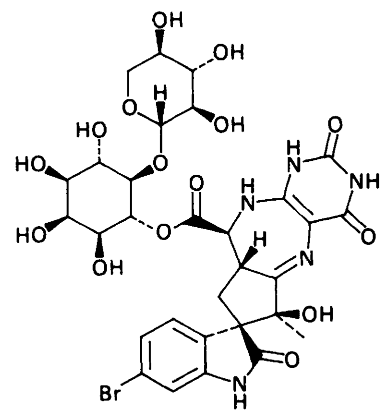
(137) $R^1,R^2 = O$

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

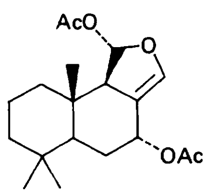
Yessotoxin (423) is a polyether metabolite from the scallop *Patinopecten yessoensis* that has been implicated in diarrhetic shellfish poisoning.[298] The structure and partial stereochemistry of yessotoxin (423) was deduced from spectral data. *Patinopecten yessoensis* also contains a series of eight polyhydroxylated sterols based on the $3\beta,5\alpha,6\beta$-cholest-7-ene (424) and $3\beta,5\alpha,6\beta,9\alpha$-cholest-7-ene (425) sterol nuclei.[299] Buccinulin (426) and the known compound kelletinin I (427), which was previously obtained from *Kelletia kelletii*,[300] have been isolated from the Mediterranean whelk *Buccinulum corneum* by two research groups.[301,302] The structure of buccinulin (426) was confirmed by synthesis.[302] Two ichthyotoxic diacylglycerols, umbraculumins A (428) and C (429), were isolated from the rare Mediterranean opisthobranch *Umbraculum mediterraneum*.[303] The Spanish dancer nudibranch *Hexabranchus sanguineus* contained dihydrohalichondramide (137) and tetrahydrohalichondramide (430), which were obtained by reduction of halichondramide (142) from the sponge *Halichondria* sp.[133] The distribution of the macrolides within the nudibranch and its egg ribbons and the defensive value of the metabolites have



(431)



(432)



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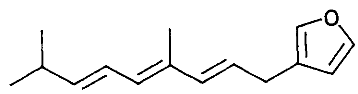

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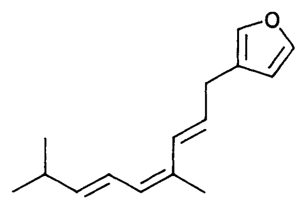

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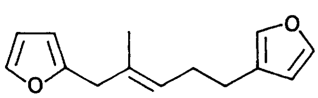

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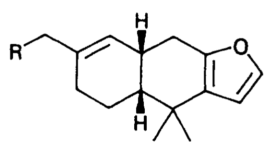
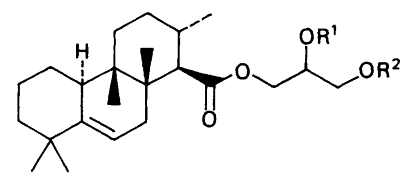
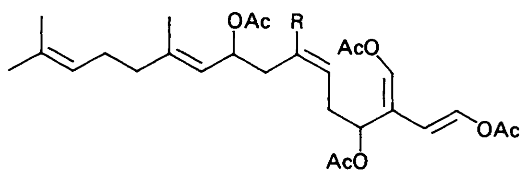


(437) R = SAc
(438) R = SMe
(439) R = –S–S–



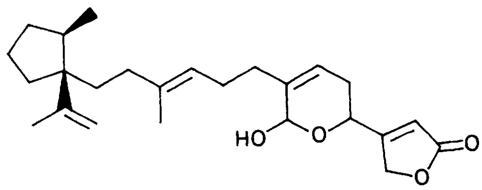
(440) R^1 = H, R^2 = Ac
(441) R^1 = Ac, R^2 = H



(442) R = CHO
(443) R = CH_2OH

been reported.[304] Pulo'upone (431), which is a metabolite of the cephalaspidean mollusc *Philinopsis speciosa*,[305] has been synthesized by two routes, both of which use an intramolecular Diels–Alder strategy.[306,307] Prosurugatoxin (432), which is a toxin from the Japanese ivory shell *Babylonia japonica*,[308] was synthesized in racemic form.[309]

The known sesquiterpene olepupuane (433)[310] has been isolated from *Dendrodoris limbata* and *D. grandiflora*.[311] The Australian nudibranch *Ceratosoma brevicaudatum* contained the known terpenes dehydrodendrolasin (434),[312] dehydrolasiosperman (435), and thiofurodysinin acetate (437),[313] and three new metabolites: *cis*-dehydrodendrolasin (436), (methylthio)furodysinin (438), and dithiofurodysinin disulfide (439).[314] These six sesquiterpenes are all assumed to be of sponge origin. The Mediterranean dorid nudibranch *Doris verrucosa* contains two ichthyotoxic diterpene glycerides, verrucosins-A (440) and -B (441), that were identified from spectral and chemical evidence and an *X*-ray determination of the structure of (441).[315] The ascoglossan *Elysia halimedae* feeds preferentially on the green seaweed *Halimeda macroloba* and modifies the major algal diterpenoid, halimadatetraacetate (442), by reduction to the corresponding alcohol (443), which it then uses as a defensive compound.[316] The metabolites of *Chromodoris funerea* collected from a marine lake in Palau were



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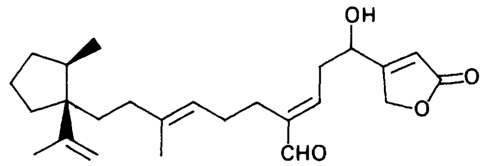
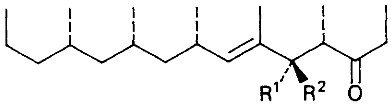
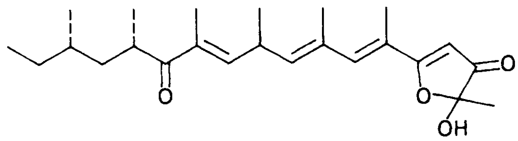


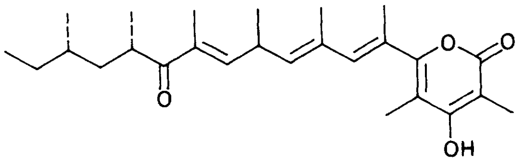
(445)



(446) $R^1,R^2 = O$
(447) $R^1 = H,\ R^2 = OH$



(448)



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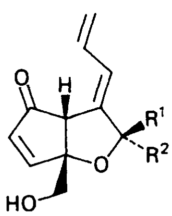
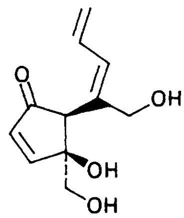


(450) $R^1 = H,\ R^2 = OH$
(451) $R^1 = OH,\ R^2 = H$
(454) $R^1 = H,\ R^2 = OMe$



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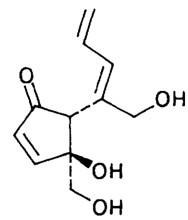

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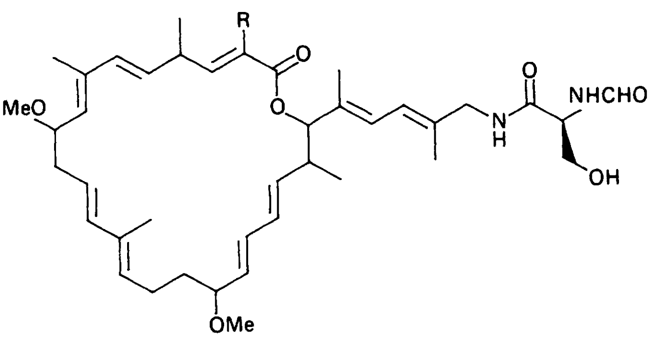


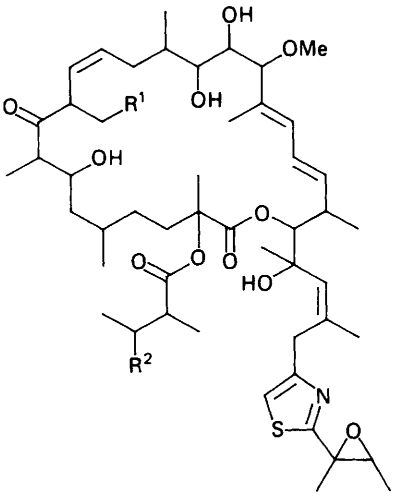
(455) R = H
(456) R = Me

quite different from those previously reported[317] from specimens taken from a nearby lagoon. Two new sesterterpenes, luffariellins-C (444) and D (445), were identified from their spectral data.[318]

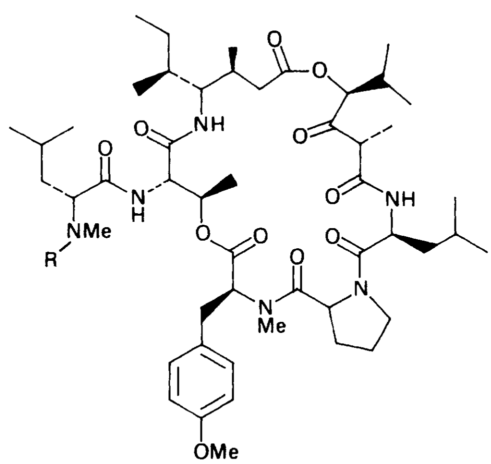
The pulmonate mollusc *Siphonaria grisea* contains two new linear polypropionate metabolites, siphonarienedione (446) and siphonarienolone (447), that were identified by interpretation of spectral data and by chemical interconversion and degradation to (2*S*,4*S*,6*S*)-nonanoic acid.[319] Aglajne-2 (448) and aglajne-3 (449) are two new propionate-derived compounds found in both *Aglaja depicta* and its prey *Bulla striata*.[320] Their structural and partial stereochemical elucidation was accomplished by using spectroscopic and chemical methods.

11 Tunicates

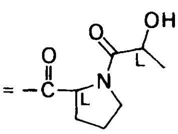
During the past year there has clearly been a surge of interest in the metabolites of tunicates. This is undoubtedly due to the high incidence of promising pharmacological properties found in the crude extracts of tunicates. The didemnenones (450)—(453) are a series of four cytotoxic cyclopentenone derivatives from didemnid tunicates.[321] Didemnenones A (450) and B (451) were isolated from *Trididemnum cyanophorum* while didemnenones C (452) and D (453) are from *Didemnum voeltzkowi*. The structures of the didemnenones were elucidated by relating their spectral properties to those of a methyl acetal derivative (454), the structure of which was determined by *X*-ray analysis. Bistramide A is a cytotoxin from *Lissoclinum bistratum* that has been partially characterized by NMR spectroscopy.[322] Two cytotoxins, iejimalides A (455) and B (456) have been isolated from an Okinawan specimen of *Eudistoma* cf. *rigida*.[323] Extensive NMR experiments were used to elucidate the structures of (455) and (456) but their relative

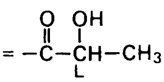


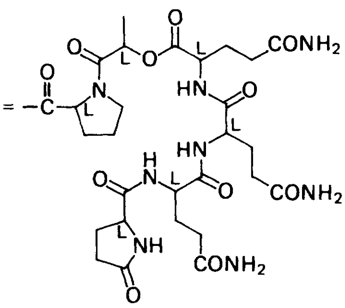
(457) $R^1 = R^2 = H$
(458) $R^1 = H$, $R^2 = OH$
(459) $R^1 = R^2 = OH$

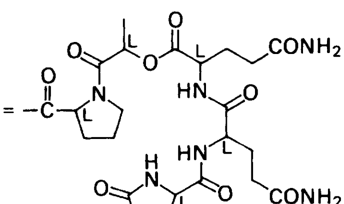


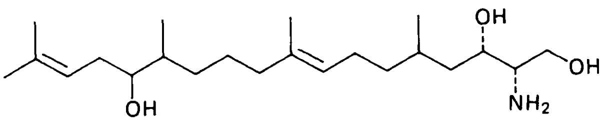
(464) R = H

(465) R = 

(466) R = 

(467) R = 

(468) R = 



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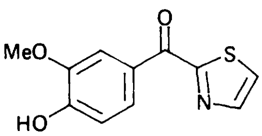

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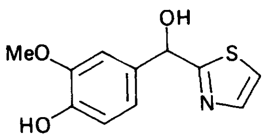
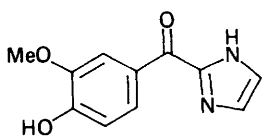
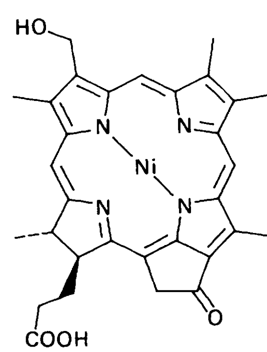


(462)



(463)

stereochemistry remains undefined. Patellazoles A (457), B (458), and C (459) are three cytotoxic macrolides from *Lissoclinum patella*. The structural elucidations of patellazole B (458)[324] and patellazole C (459)[325] depend on the interpretation of spectral data that did not permit stereochemical assignments. The 2,3-*threo*-13,14-*erythro*-stereochemistry of aplidiaspingosine (460), which is an antimicrobial and cytotoxic terpenoid from a species of *Aplydium*,[326] has been defined by total synthesis.[327] The structures of two thiazoles, (461) and (462), and an imidazole (463) from *Aplydium pliciferum* were elucidated by interpretation of spectral data and confirmed by synthesis.[328] A high-yielding two-phase cyclization reaction has been employed in a synthesis of didemnins A (464), B (465), and C (466).[329,330] The structural revision, total syntheses and pharmacological properties of didemnins A—E (464)—(468), which are cytotoxic, antiviral, and immunosuppressive agents from *Trididemnum solidum*, have been reviewed.[331] The same review reports the structural elucidation of tunichlorin (469), which is a nickel-containing blue-green coloured porphynoid.



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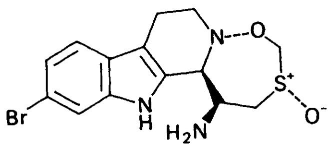

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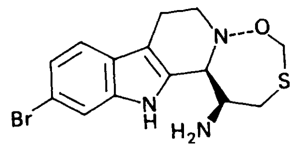

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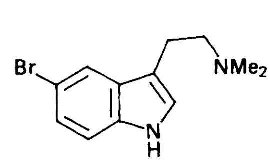

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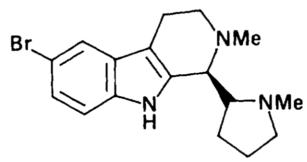
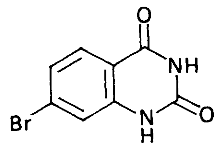
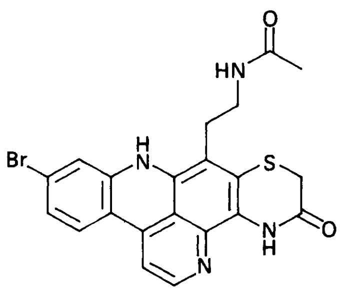


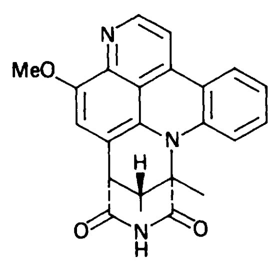
(473)



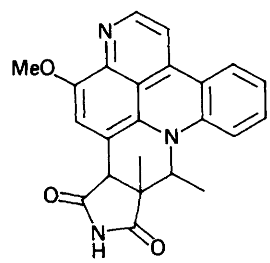
(474)



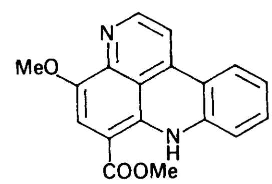
(475)



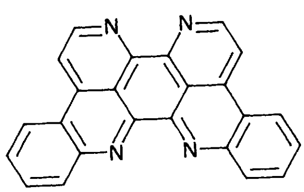
(476)



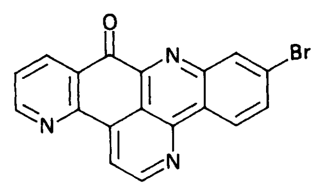
(477)



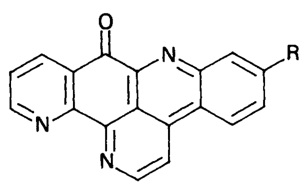
(478)



(479)



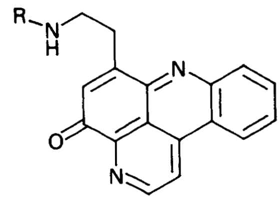
(480)

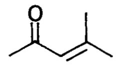


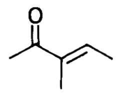
(481) R = Br
(482) R = H

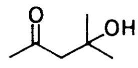
Eudistomin K sulphoxide (470), which is an antiviral agent from the New Zealand ascidian *Ritterella sigillinoides*,[332] has been synthesized from eudistomin K (471), the structure and absolute configuration of which were determined by *X*-ray analysis.[333] *Eudistoma fragum* contained *N*,*N*-dimethyl-5-bromotryptamine (472), which had previously been found in the sponge *Smenospongia aurea*,[334] and a new alkaloid, woodinine (473), the structure of which was proposed on the basis of its spectral properties.[335] The structure of 7-bromo-2,4(1*H*,3*H*)-quinazolinedione (474), which accompanies 6-bromoindole-3-carboxaldehyde in *Pyura sacciformis*, has been confirmed by synthesis.[336]

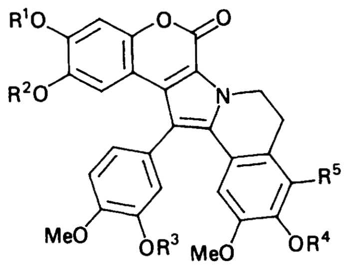
The structure of shermilamine A (475), which is an orange pigment from a species of *Trididemnum* from Guam, was determined by *X*-ray analysis.[337] A group of three somewhat similar alkaloids – segoline A (476), isosegoline A (477), and nor-segoline (478) – were obtained from a Red Sea species of *Eudistoma*.[338] The structure of segoline A (476) was determined by *X*-ray analysis and the remaining structures were proposed on the basis of comparison of spectral data. A second collection of the same species of *Eudistoma* from Eilat contained eilatin (479), the structure of which was determined by *X*-ray analysis.[339] The structure (480) that was assigned by interpretation of long-range C/H coupling data to 2-bromoleptoclinidinone,[340] which is an alkaloid from a species of *Leptoclinides*, is now known to be incorrect. The correct structure of 2-bromoleptoclinidinone (481)[341] is that of a brominated derivative of ascididemnin (482), which is a cytotoxic alkaloid from an Okinawan species of *Didemnum*.[342] The structure of ascididemnin (482) was elucidated by interpretation of spectral data. Cystodytins A (483), B (484), and C (485) are tetracyclic alkaloids from *Cystodytes dellechiajei* that exhibit potent antineoplastic activity.[343] The structures of the cystodytins (483)—(485) were elucidated by interpretation of spectral data.



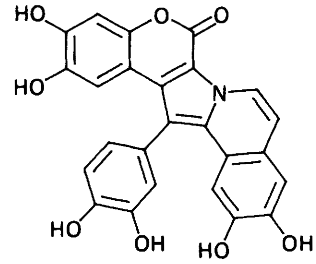
(483) R = 

(484) R = 

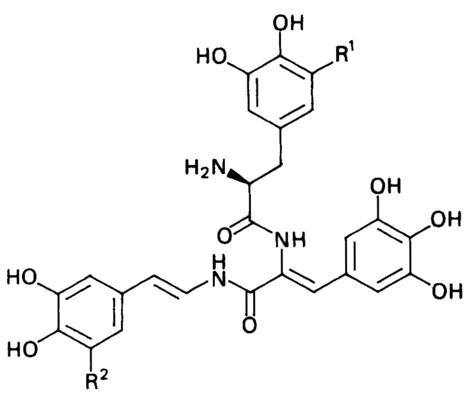
(485) R = 



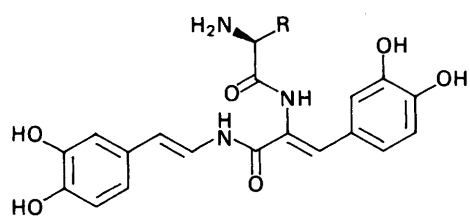
(486) $R^1 = R^3 = H$, $R^2 = R^4 = Me$, $R^5 = OH$
(487) $R^1 = H$, $R^2 = R^3 = R^4 = Me$, $R^5 = OH$
(488) $R^1 = Me$, $R^2 = R^3 = R^4 = R^5 = H$



(489)



(490) $R^1 = R^2 = OH$
(491) $R^1 = H$, $R^2 = OH$
(492) $R^1 = R^2 = H$

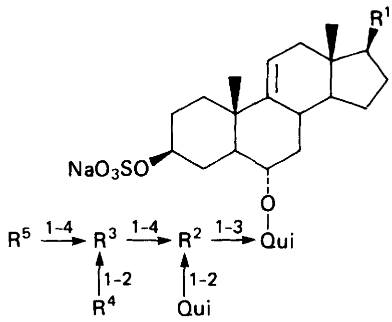


(493) R = H
(494) R = *i*-Bu

The ascidian *Didemnum characeum* contained a series of four alkaloids (486)—(489) that are closely related to the lamellarins[344] previously found in the prosobranch mollusc *Lamellaria* sp. The structure of lamellarin E (486) was determined by *X*-ray analysis and those of lamellarins F (487), G (488), and H (489) were elucidated by interpretation of spectral data.[345] The tunichromes are a series of reducing blood pigments from *Ascidia nigra* and *Molgula manhattensis*.[346] The structures of the very unstable tunichromes *An*-1 (490), *An*-2 (491), *An*-3 (492), *Mm*-1 (493), and *Mm*-2 (494) were deduced by spectral analyses. Evidence of complex formation between vanadium and the tunichromes is presented but a stable complex was not isolated.

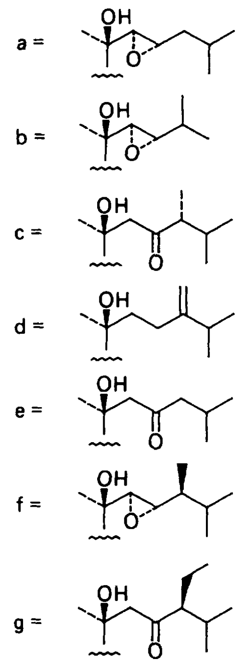
12 Echinoderms

The sea stars continue to yield new saponins and polyhydroxylated sterols but these compounds are predominantly minor variations of familiar structural types. A review of the secondary metabolites of echinoderms was particularly useful because of its coverage of the Russian literature.[12] In addition to known saponins, the Pacific sea star *Asterias amurensis*

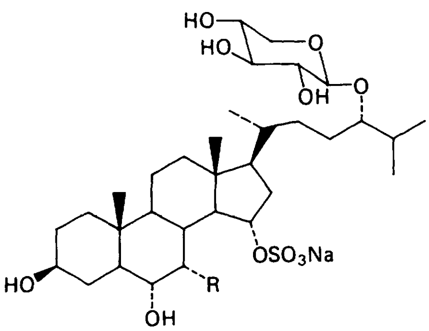


(495) R^1 = a, R^2 = Xyl, R^3 = Gal, R^4 = Qui, R^5 = H
(496) R^1 = b, R^2 = Xyl, R^3 = Gal, R^4 = Qui, R^5 = H
(497) R^1 = c, R^2 = Xyl, R^3 = Gal, R^4 = Qui, R^5 = H
(498) R^1 = d, R^2 = Xyl, R^3 = Glu, R^4 = Qui, R^5 = H
(503) R^1 = e, R^2 = Qui, R^3 = Glu, R^4 = Fuc, R^5 = H
(504) R^1 = f, R^2 = Xyl, R^3 = Glu, R^4 = Fuc, R^5 = Gal
(505) R^1 = g, R^2 = Xyl, R^3 = Glu, R^4 = Fuc $\xrightarrow{1-3}$ Fuc, R^5 = H
(506) R^1 = h, R^2 = Qui, R^3 = Glu, R^4 = Fuc, R^5 = H

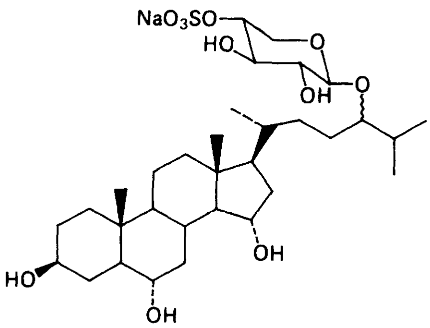
Fuc = fucose, Gal = galactose, Qui = quinovose, Xyl = xylose; all sugars are in the pyranose form and linkages are β.



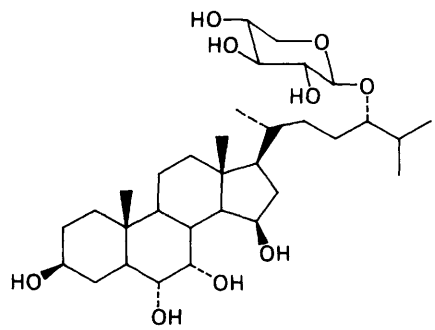
h = $-COCH_3$



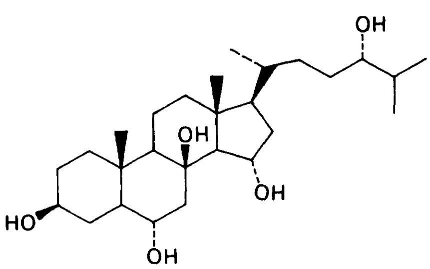
(499) R = H
(500) R = OH



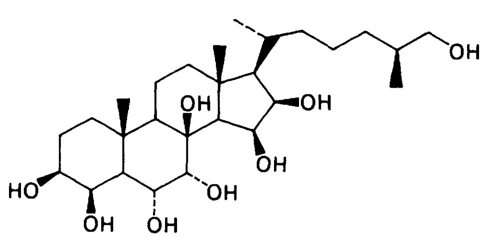
(501)



(502)

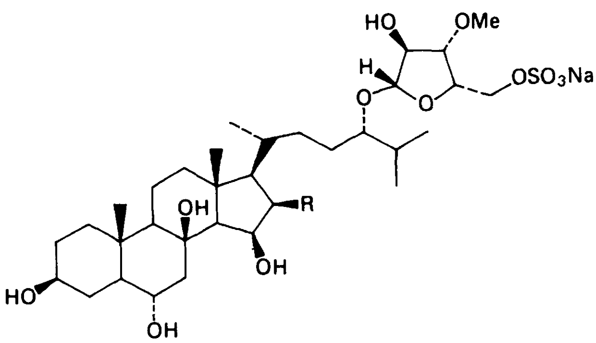


(507)

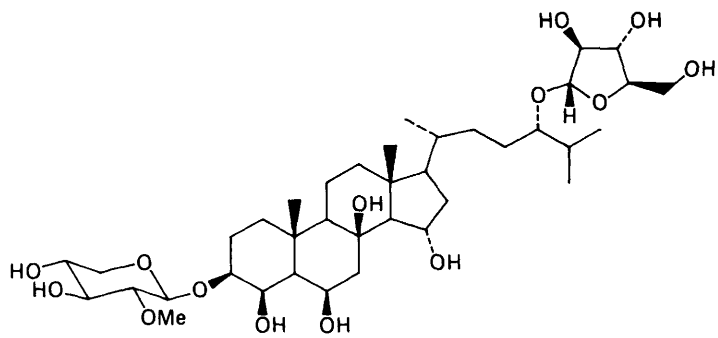


(508)

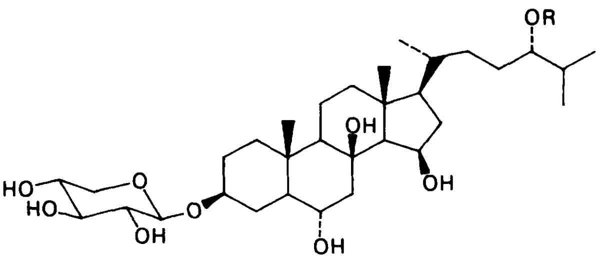
contained four new saponins – asterosides A (495), B (496), C (497), and D (498) – that differ primarily in the structures of their steroidal side chains.[347] The same sea star also contains four new polyhydroxysteroidal glycosides; amurensosides A (499), B (500), C (501), and D (502).[347] The Japanese sea star *Asterina pectinifera* likewise contains four new saponins – pectiniosides A (503), B (504), C (505), and D (506)[348,349] – and two new polyhydroxylated steroids: (24*S*)5α-cholestane-3β,6α,8,15α,24-pentol (507) and (25*S*)-5α-cholestane-3β,4β,6α,7α,8,15β,16β,26-octol (508).[350]



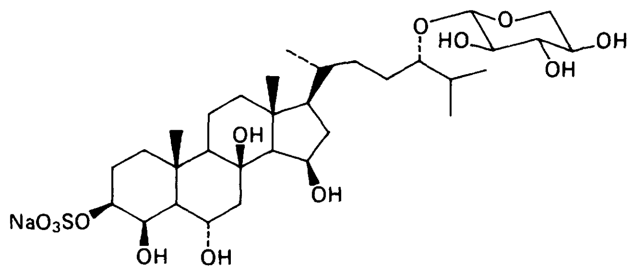
(509) R = H
(510) R = OH



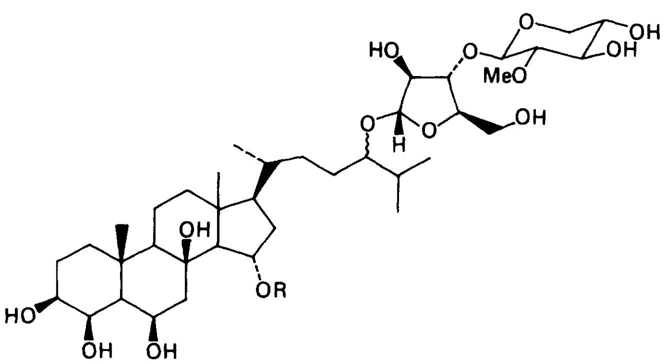
(511)



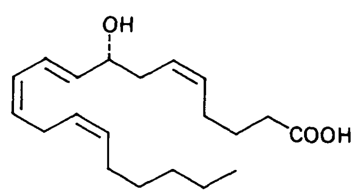
(512) R = SO_3Na
(514) R = β-Xyl(p)
(515) R = β-Xyl(p), 22(23)*E*-dehydro
(516) R = β-Glu(p)



(513)



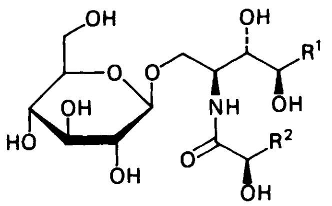
(517) R = Ac
(518) R = H



(519)

A number of new polyhydroxysteroidal glycosides have been reported. Indicosides B (509) and C (510) were isolated from *Astropecten indicus*,[351] thromidioside (511) was found in *Thromidia catalia*,[352] and glacialosides A (512) and B (513) were obtained from *Marthasterias glacialis*.[353] All of these compounds are minor metabolites and were accompanied by known saponins. The North Pacific sea star *Distolasterias nipon* contains asterosaponins D_1 (514), D_2 (515), and D_3 (516),[354] while specimens of *Echinaster sepositus* from Madagascar provided echinasterosides B_1 (517) and B_2 (518), both of which contain an unusual 1 → 3 glycosidic linkage.[355]

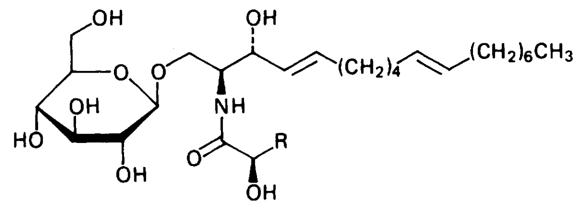
The eicosanoids 8-(*R*)-HETE (519) and the corresponding 17,18-didehydro derivative have been found in *Patiria miniata*.[356] This finding is of interest since it was known that 8-(*R*)-HETE (519) can trigger oocyte maturation in starfish.[357] Studies of the glycosphingolipids from *Acanthaster planci* have



(520) $R^1 = C_{12}H_{25}$, $R^2 = C_{22}H_{45}$

(521) $R^1 = C_{18}H_{37}$, $R^2 = C_{14}H_{29}$

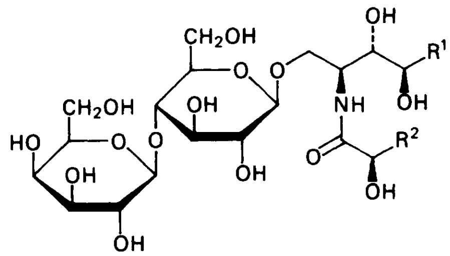
(522) $R^1 = -(CH_2)_8CH\overset{Z}{=}CH-C_8H_{17}$, $R^2 = C_{14}H_{29}$



(523) $R = C_{20}H_{41}$

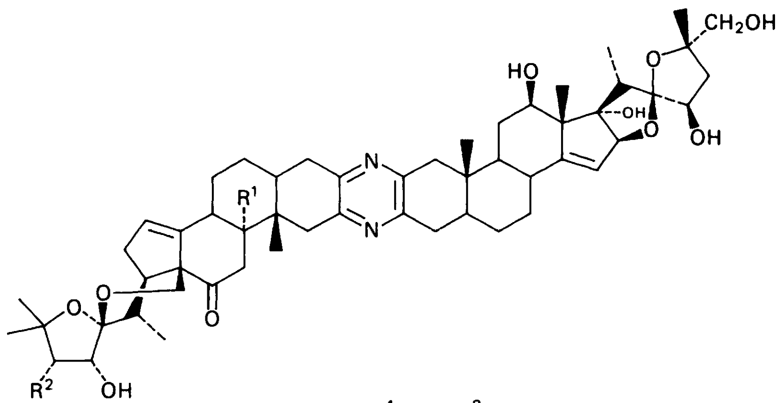
(524) $R = C_{21}H_{43}$

(525) $R = C_{22}H_{45}$



(526) $R^1 = C_{12}H_{25}$, $R^2 = C_{22}H_{45}$

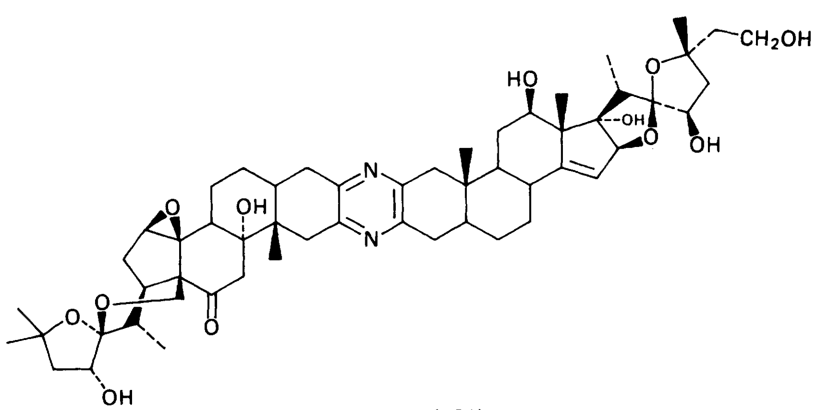
(527) $R^1 = -(CH_2)_8 \cdot CH\overset{Z}{=}CH \cdot C_8H_{17}$, $R^2 = C_{14}H_{29}$



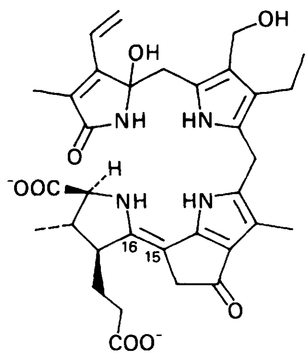
(528) $R^1 = H$, $R^2 = H$

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

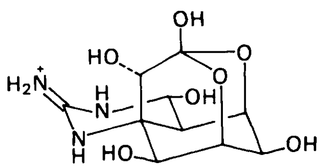
(530) $R^1 = OH$, $R^2 = Me$



(531)



(532)



(533)

yielded six new cerebrosides, acanthacerebrosides A—F (520)—(525),[358,359] and two new ceramide lactosides, acanthalactosides A (526) and B (527).[360]

13 Miscellaneous

The cytotoxic constituents of the marine worm *Cephalodiscus gilchristi* (Pterobranchia) have been identified as pyrazine alkaloids derived from two different steroidal subunits. The structure of cephalostatin 1 (528) was determined by *X*-ray crystallographic analysis[361] and the structures of cephalostatins 2 (529), 3 (530), and 4 (531) were elucidated by interpretation of spectral data.[362,363]

The fluorescent compound in the shrimp *Euphausia pacifica* was found to be the bile pigment (532).[364] Compound F (532) was identified by interpretation of spectral data, chemical conversions, and synthesis of a degradation product. The stereochemistry of the 15,16-olefinic bond was not determined.

A new tetrodotoxin derivative, 11-nortetrodotoxin (533), has been isolated as a minor constituent of the liver of the pufferfishes *Fugu niphobles*, *F. pardalis*, and *F. poecilonotus*.[365]

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