*Nat. Prod. Rep.*, 2003, **20**, 1-48

# Marine natural products

**John W. Blunt**,[a*] **Brent R. Copp**,[b] **Murray H. G. Munro**,[a] **Peter T. Northcote**[c] **and Michèle R. Prinsep**[d]

[a]*Department of Chemistry, University of Canterbury, Christchurch, New Zealand*

[b]*Department of Chemistry, University of Auckland, Auckland, New Zealand*

[c]*School of Chemical and Physical Sciences, Victoria University of Wellington, Wellington, New Zealand*

[d]*Department of Chemistry, University of Waikato, Hamilton, New Zealand*

***Received (in Cambridge, UK) 31st October 2002***

***First published as an Advance Article on the web 19th December 2002***

This review covers the literature published in 2001 for marine natural products, with 495 citations (365 for the period January to December 2001) referring to 793 compounds isolated from marine microorganisms and phytoplankton, green algae, brown algae, red algae, sponges, coelenterates, bryozoans, molluscs, tunicates and echinoderms. The emphasis is on new compounds (680 for 2001), together with their relevant biological activities, source organisms and country of origin. Syntheses that confirm or revise structures or

* Corresponding author: j.blunt@chem.canterbury.ac.nz

stereochemistries have been included (113), including any first total syntheses of a marine natural product.

Covering: 2001. Previous review: 2002, **19**, 1.



## 1 Introduction

Since the appearance of the first of these reviews of marine natural products in the first issue of Natural Products Reports in 1984,[1] a further 17 reviews have appeared, with 13 annually

since 1990. All have been meticulously prepared by Professor D. John Faulkner, following his original review of the area in Tetrahedron in 1977.[2] These reviews have become the most highly cited articles for this journal and are clearly very important for the marine natural products community, undoubtedly an outcome of the comprehensiveness, accuracy and readable style developed and maintained by Professor Faulkner. John has now relinquished the task of preparing these reviews. It is with some trepidation that we have agreed to take over the task for assembling the review. Foremost in our minds is the need to maintain the high standards that have been set in the past. The marine natural products community, and others with an interest in the area, are indebted to Professor Faulkner for his work on these reviews. He has not entirely given away his interest in these reviews however, and we acknowledge the support and information he has provided in assisting us to prepare the 2001 review. For this review we have chosen to follow the same style and layout seen in the previous reviews. There has been continued growth in the reports from studies on microorganisms, and on synthetic efforts on marine natural products. In this review, we have included papers on syntheses if they provide new information on the stereochemistry of previously reported compounds, or provide for a revision of structure. We also report the first total synthesis of any marine natural product. In view of the rapid growth in this area, we believe that it would be timely to dedicate a companion review to this topic and we are currently arranging to do this.

A number of reviews on a variety of topics appeared in 2001. One group covered natural products from many sources including marine organisms: “Natural products in anticancer therapy”,[3] “Endophytes: a rich source of functional metabolites”,[4] “Simple indole alkaloids and those with nonrearranged monoterpenoid unit”,[5] “Diterpenoids”,[6] “Biologically active proteins from natural product extracts”[7] and “Natural product-based anti-HIV drug discovery and development facilitated by the NCI Developmental Therapeutics Program”.[8]

Cyanobacteria have been well covered by "Marine cyanobacteria – a prolific source of natural products",[9] "The toxins of cyanobacteria",[10] and "Nitrogen-containing metabolites from marine cyanobacteria".[11] Ascidian-derived compounds are partially reviewed in "Recent advances on the research of natural products of ascidians".[12] Specific compounds have been reviewed in "Chemistry of potent anticancer compounds, amphidinolides",[13] "Distribution and origin of tetrodotoxin",[14] the mini-review "Domoic acid: a fascinating marine toxin",[15] and "Pectenotoxins – an issue for public health",[16] while specific compound classes have been covered in "Recent advances in study on cyclic peptides from marine sponges",[17] "Aquatic animal carotenoids",[18] "Advances in marine natural products of the indole and annelated indole series: chemical and biological aspects",[19] and "Marine sulfur-containing natural products"[20] which describes the 482 sulfur-containing compounds (excluding sulfates) reported from 1985-1999. Some ecological and taxonomic aspects are reviewed in "Secondary metabolites from Antarctic marine organisms and their ecological implications",[21] "Marine chemical ecology: applications in marine biomedical prospecting",[22] and "Marine natural products chemistry as an evolutionary narrative"[23] which includes a taxonomic survey. Other reviews include "Biologically active compounds from marine organisms",[24] "Marine bioprospecting – trawling for treasure and pleasure"[25] which highlights the molecular diversity seen in the results obtained by the University of Melbourne's marine natural product group, "Marine pharmacology in 1999: antitumor and cytotoxic compounds"[26] which describes the structures reported in 1999 for 30 antitumour and cytotoxic compounds, and "Marine organisms as a source of new anticancer agents"[27] which summarises current preclinical and clinical trial data for a range of marine natural products. Volume 6 of "Recent Advances in Marine Biotechnology" contains a series of reviews: "Novel pharmaceutical compounds from marine bacteria",[28] "Recent developments on antimicrobial metabolites from marine sponges",[29] "Bioactive compounds from hard

corals",[30] "Novel bioactive compounds from the soft corals: Chemistry and biomedical applications",[31] "Pore-forming proteins from sea anemones and the construction of immunotoxins for selective killing of harmful cells",[32] "Bioactive compounds from bryozoans",[33] "Novel alkaloids from marine bryozoans",[34] "Ion channel toxins as molecular models for the design of new drugs",[35] "Proteinases from marine organisms"[36] and "Cooperative antifoulant testing: A novel multisector approach".[37] A new database of 8,000 natural products has been introduced in "Using XML in the marine natural products database",[38] while the MarinLit database[39] continues to be updated, and has been used for the preparation of this review.

## 2 Marine microorganisms and phytoplankton

There continues to be much interest in cultured marine organisms. An acidic polysaccharide isolated from *Pseudoalteromonas distincta* that was obtained from a marine sponge, contained two unusual acidic amino sugars; 2-acetamido-2-deoxy-D-galacturonic acid **1** and 5-acetamido-3,5,7,9-tetradeoxy-7-formamido-L-*glycero*-L-*manno*-nonulosonic acid **2**.[40] A *Streptomyces* sp. isolated from a shallow sea sediment near Livingston Island, Antarctica was the source of 2-amino-9,13-dimethyl heptadecanoic acid **3,** a compound with selective antimicrobial activity.[41] The culture broth of a *Streptomyces* sp. isolated from sediment collected in Korean waters, yielded six novel lactone-containing metabolites **4**-**9**.[42] A novel glycerol diether, 2,3-di-*O*-dihydro-14,15-geranylgeranyl-*sn*-glycerol **10**, was isolated from an anaerobic culture of the archaeon *Thermococcus* sp., collected from a deep-sea hydrothermal vent.[43] A cell-free culture of the marine bacterium *Vibrio angustum* was the source of the ether 1-(2'-methylpropoxy)-2-hydroxy-2-methylpropoxylbutane **11**, which induced both the acylated homoserine lactone (AHL) regulatory system in *Agrobacterium tumefaciens* and

bioluminescence in *Vibrio harveyi*.[44] Macrolactins G-M **12**-**18** were isolated from a culture broth of a *Bacillus* sp. The strain had been isolated from the red alga *Schizymenia dubyi* collected from Japanese waters and also contained macrolactins A and F which were previously isolated from an unclassifiable deep-sea bacterium.[45] The macrolactins exhibited selective antimicrobial activity.[46] A bacterial isolate from the tissues of an unidentified tube worm collected off Papua New Guinea that was tentatively identified as *Bacillus laterosporus* yielded the cationic peptide bogorol A **19**. This compound displayed reasonably potent activity against both methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcal strains (VRE) of bacteria but exhibited no activity against a range of other bacteria and fungi.[47] A novel β-methoxyacrylate antibiotic possessing a conjugated tetraene moiety was isolated from the culture broth of the marine myxobacterium *Haliangium luteum* and named haliangicin **20**. Haliangicin was susceptible to oxidation in air and had to be kept in solution at –20 °C due to rapid decomposition at room temperature when evaporated to dryness.[48] Haliangicin inhibited growth of a wide range of fungi but was inactive against bacteria.[49] Micromonospolides A-C **21**-**23**, macrolides containing a 16-membered lactone ring, were isolated from an undescribed actinomycete *Micromonospora* sp. These compounds inhibited the gastrulation of starfish (*Asterina pectinifera*) embryos.[50,51] The crude extract of a halophilic actinomycete, the new species *Micromonospora lomaivitiensis*, that was isolated from the inner core of the ascidian *Polysyncraton lithostrotum*, exhibited potent DNA-damaging activity in the biochemical induction assay (BIA) and potent cytotoxicity against a panel of cancer cell lines. Two dimeric diazobenzofluorene glycosides, designated as lomaiviticins A **24** and B **25**, were isolated from the extract by BIA-guided fractionation. Both were demonstrated to be potent DNA-damaging agents and lomaiviticin A **24** was shown to cleave double stranded DNA under reducing conditions. Lomaiviticin A possessed a unique cytotoxicity profile as compared to

known DNA-damaging drugs such as adriamycin and mitomycin C against a number of cancer cell lines. Both lomaiviticins A and B exhibited potent antibacterial activity against *S. aureus* and *Enterococcus faecium*.[52] A total synthesis of thiocoraline **26**, a potent anti antibiotic that was isolated from *Micromonospora* sp.,[53,54] has been accomplished and the relative and absolute stereochemistry established. Thiocoraline was also shown to bind to DNA by high-affinity bisintercalation, but with no obvious sequence selectivity. Thiocoraline was exceptionally cytotoxic to the L1210 murine leukaemia cell line with an $IC_{50}$ value of 200 pM.[55] The kahakamides A **27** and B **28** are new indole nucleosides that were isolated from the actinomycete *Nocardiopsis dassonvillei*, obtained from a shallow water sediment sample from Kauai, Hawaii. Kahakamide A **27** exhibited slight inhibition of *B. subtilis* in a disc-diffusion assay.[56] (*Z*,*Z*)-4,8-Dihydroxy-undeca-2,9-dienedioic acid diamide **29** was obtained from an unidentified marine actinomycete.[57]

Marine-sourced fungi continue to be of interest. A total synthesis of (±)-epoxysorbicillinol **30**, a pigment isolated from the fungus *Trichoderma longibrachiatum* that was separated from a *Haliclona* sponge,[58] has been accomplished in 13 steps from diethyl methylmalonate.[59] The sesquiterpene lactone, 8-hydroxy-9-one-7(11)-eremophilien-12,8-olide **31** was isolated from the marine fungus *Hypoxylon oceanicum* from the South China Sea.[60] The isocoumarin avecennin A **32** was isolated from a mangrove endophytic fungus from the South China Sea,[61] while the mangrove fungus *Xylaria* sp., also from the South China Sea, yielded xyloketals A-E **33**-**37**. Xyloketal A **33** is a potent inhibitor of acetylcholine esterase.[62] The unusual allenic ether, xyloallenolide A **38**, was isolated from a *Xylaria* sp. from the South China Sea along with an aromatic allenic ether **39** which had not been previously reported from a natural source.[63] Chlorogentisylquinone **40** was isolated from the culture broth of an unidentified marine fungus, and was shown to inhibit sphingomyelinase activity of rat brain membranes.[64] The marine fungus *Aspergillus*

*versicolor,* isolated from the sponge *Xestospongia exigua* from Bali, was the source of six chromone derivatives, the aspergiones A-F **41**-**46**,[65] and four further compounds, aspergillone **47**, aspergillodiol **48**, aspergillol **49** and 12-acetyl-aspergillol **50**.[66] An inhibitor of anaerobic electron transport, nafuredin **51**, was isolated from *Aspergillus niger*, isolated from a marine sponge collected in Palau. Nafuredin proved to be a highly selective inhibitor of NADH-fumarate reductase (NFRD) from the pig roundworm *Ascaris suum*. Biosynthetic studies of nafuredin were carried out.[67] The alkaloid circumdatin G **52** was isolated from the culture broth of the fungus *Aspergillus ochraceus,* isolated from sediment collected in the Sea of Japan.[68] A new macrocyclic trichothecene, 12,13-deoxyroridin E **53** was isolated from the filamentous fungus *Myrothecium roridium* that was obtained from woody material collected in Palau. 12,13-Deoxyroridin E was active against human leukaemia HL-60 and murine L1210 cell lines.[69] The macrosphelides E-I **54**-**58** have been isolated from *Periconia byssoides,* separated from the sea hare *Aplysia kurodai*. The absolute stereostructures of the macrosphelides were determined on the basis of spectroscopic analyses and chemical transformations. The absolute configuration of the known compound macrosphelide C **59** was established by X-ray analysis and application of the modified Mosher method. Macrosphelides E-H **54**-**57** inhibited the adhesion of HL-60 cells to human umbilical vein endothelial cells (HUVEC).[70] The absolute stereochemistry of spiroxin A **60**, a DNA-cleaving bisnaphthospiroketal from a marine-derived fungus,[71] has been determined as (2*S*,3*R*,4*S*,2'*S*,3'*R*,4'*S*) by application of the exciton chirality method following derivatisation.[72] A *Pestalotia* species of fungus isolated from the surface of the brown alga *Rosenvingea* sp. from the Bahamas, produced a chlorinated benzophenone antibiotic pestalone **61** only when a unicellular marine bacterium was co-cultured in the fungal fermentation. It was not detected when either organism was cultured individually. Pestalone **61,** whose structure was confirmed by X-ray analysis, exhibited only moderate *in vitro*

cytotoxicity in the National Cancer Institute's (NCI) 60 human tumour cell line panel but showed potent activity against MRSA and VCE.[73] A culture broth of the marine fungus *Halorosellinia oceania* collected in Thailand was the source of an ophiobolane sesterterpene halorosellinic acid **62** and of 4-methyl-2-hexylidene-3-methylsuccinate **63**. The relative stereochemistry of halorosellinic acid was assigned by analysis of NOESY data. Halorosellinic acid **62** exhibited moderate antimalarial activity against *Plasmodium falciparum* but only weak antimycobacterial activity.[74] 3-Methyl-6,8-methoxy-2-aza-9,10-anthraquinone (scorpinone) **64** was isolated from the mycelium of a cultured *Bispora*-like fungus from sediment collected in the Bahamas, and the structure determined by X-ray analysis.[75] Investigations of cultures of the mycelium of an unidentified fungus isolated from the red alga *Ceradictyon spongiosum* in Okinawa resulted in the isolation of two linear dodecapeptides, dictyonamides A **65** and B **66**. Dictyonamide A **65** inhibited cyclin-dependent kinase 4 while dictyonamide B **66** was inactive.[76] Hortein, **67**, was isolated from the fungus *Hortaea werneckii* obtained from the Mediterranean sponge *Aplysina aerophoba*. Hortein possesses an acenaphthol[1',2':7,8]naphthalene ring system which is unique among natural products.[77] Cultures of *Cladosporium herbarum* isolated from the sponge *Callyspongia aerizusa* collected from Bali yielded the 12-membered macrolide pandangolide 3 **68**, the macrolide dimer pandangolide 4 **69** and a new acetyl derivative **70** of 5-hydroxymethyl-2-furancarboxylic acid, (also known as Sumiki's acid). Compound **70** inhibited the growth of *B. subtilis* and *S. aureus* in an agar plate diffusion assay.[78] The penochalasins D-H **71**-**75** were isolated from a strain of *Penicillium* sp. originally separated from the green alga *Enteromorpha intestinalis*. The compounds were all moderately cytotoxic to P388 murine leukaemia cells.[79]

Cyanobacteria continue to yield novel structures. Apratoxin A **76**, a cyclic depsipeptide of mixed peptide-polyketide origin, has been isolated from the cyanobacterium

*Lyngbya majuscula* collected from Guam. The absolute configurations of the amino acid-derived units were determined by chiral HPLC analysis of hydrolysis products. The absolute stereochemistry of the new dihydroxylated fatty acid unit, 3,7-dihydroxy-2,5,8,8-tetramethylnonanoic acid was established through analysis by Mosher's method. The solution conformation of apratoxin A **76** was mimicked by molecular modelling. Apratoxin A exhibited potent cytotoxicity *in vitro* against KB and LoVo cell lines but was toxic *in vivo* to mice and was poorly tolerated.[80] A different population of *L. majuscula* from Guam was the source of two further cyclic depsipeptides, pitipeptolides A **77** and B **78**. Pitipeptolides A and B exhibited weak cytotoxicity against LoVo cells and both compounds were active in the antimycobacterial diffusion susceptibility assay but were less active than a control. Pitipeptolides A and B also stimulated elastase activity.[81] Antillatoxin B **79**, an *N*-methyl homophenylalanine analogue of antillatoxin,[82] was isolated from samples of *L. majuscula* from Puerto Rico and the Dry Tortugas. Antillatoxin B was ichthyotoxic to goldfish and activated sodium channels in mouse neuro-2a neuroblastoma cells.[83] A Panamanian collection of *L. majuscula* was the source of four new metabolites, pseudodysidenin **80**, dysidenamide **81**, nordysidenin **82** and dragonamide **83**. The first three of these are closely related to dysidenin[84] and isodysidenin,[85] isolated from the sponge *Dysidea herbacea*. This is the first reported instance of the isolation of such compounds from a free-living cyanobacterium, most likely indicating that similar metabolites isolated from sponges are metabolites of associated cyanobacteria. Dragonamide contains a unique C8-alkynoate unit.[86] Somamides A **84** and B **85** were isolated from mixed assemblages of the cyanobacteria *L. majuscula* and *Schizothrix* sp. from Fiji. The absolute stereochemistries of the amino acid residues were determined by Marfey's analysis. These depsipeptides are analogous to symplostatin 2, isolated from the cyanobacterium *Symploca hydnoides*[87] and dolastatin 13, originally isolated from the sea hare *Dolabella auricularia*[88] but most likely originating from

its cyanobacterial diet.[89] The first total synthesis of lyngbyabellin A **86**, a peptolide isolated from *L. majuscula* from Guam,[90] has been described. Lyngbyabellin A was synthesised in 58% yield by a convergent strategy.[91] A culture of the marine cyanobacterium *Oscillatoria* sp. yielded a diacylgalactolipid **87**.[92] The total stereochemistry of symplostatin 1 **88**, a metabolite of *Symploca hydnoides*,[93] was completed by determination of the stereochemistry of the *N,N*-dimethylisoleucine units to be (*S,S)*.[94] The same paper reported the isolation of dolastatin 10 from a *Symploca* species, suggesting that cyanobacteria are the ultimate producers of this metabolite, rather than the sea hare *Dolabella auricularia* from which it was originally isolated.[95] Symplostatin 1, a microtubule inhibitor, was a very potent cytotoxin both *in vitro* (KB and LoVo cell lines) and *in vivo* (with mice). It was, however, very toxic, causing lethality on day 1 when injected intravenously at low doses.[94] Seven compounds, **89**-**95**, of which five were polychlorinated acetamides, were isolated from *Microcoleus lyngbyaceus* collected from Chuuk, Micronesia. Compound **95** was tentatively identified as an aminotridecane but the placement of the amino group could not be determined as the compound decomposed before mass spectral studies could be carried out. A positional isomer of compound **93** was synthesised in six steps from δ-decanolactone.[96]

Stereoselective synthesis of an HI/JK ring model of prymnesins 1 and 2, glycosidic toxins isolated from the red tide phytoflagellate *Prymnesium parvum,*[97] was accomplished. Comparison of the NMR data with those of the natural toxins confirmed the original stereochemical assignments.[98] The first total synthesis of euplotin A **96**, a cytotoxin of the ciliated protist *Euplotes crassus*[99] has been achieved. The synthetic strategy employed retro-cycloaddition reactions of readily available 5-acyl-4-alkyl-4*H*-1,3-dioxins.[100] Ostreocin D **97**, a new analogue of palytoxin, was isolated from the dinoflagellate *Ostreopsis siamensis*. The structure was determined as 42-hydroxy-3,26-didemethyl-19,44-dideoxypalytoxin by 2D NMR analysis of ostreocin D and the ozonolysis products.[101] 3D Fourier transform and

gradient enhanced NMR spectroscopies allowed the full assignment of the $^{1}H$ and $^{13}C$ NMR spectra of palytoxin **98** and the *N*-acetylpalytoxin analogue **99**. Notably, the $^{15}N$ NMR spectrum of *N*-acetylpalytoxin **99** could be assigned without $^{13}C$ or $^{15}N$ enrichment.[102] The modestly cytotoxic (L1210 and KB cell lines) amphidinolides T2 **100**, T3 **101** and T4 **102**, 19-membered macrolides structurally related to amphidinolide T1,[103] have been isolated from two strains of the dinoflagellate *Amphidinium* sp.[104] The absolute configurations of **100**-**102** and of amphidinolide T1 **103** were determined by comparison of NMR spectroscopic data with those of synthetic model compounds. The biosynthetic origin of amphidinolide T1 **103** was probed using singly and doubly labelled $^{13}C$ sodium acetate and $^{13}C$-labelled sodium bicarbonate. Results suggested that amphidinolide T1 **103** was generated through nonsuccessive mixed polyketides and that the main carbon source of amphidinolide T1 was derived from carbon dioxide. Amphidinolide T5 **104** was later isolated from the same extract of *Amphidinium* sp., and the stereostructure of amphidinolide T1 **103** was confirmed by a X-ray analysis.[105] The absolute stereochemistry of amphidinolide C **105**, a 25-membered macrolide from *Amphidinium* sp.[106] was determined by a combination of NMR spectroscopic analyses, degradation experiments and synthesis of the C1-C7 segment.[107] The first total synthesis of the related 19-membered lactone amphidinolide K **106**[108] has been accomplished. The stereochemistry of the synthetic material was confirmed by X-ray analysis to establish the absolute stereochemistry of the natural product.[109]

Spirolides A **107**, C **108** and 13-desmethyl spirolide C **109** were isolated from the annual accumulation of contaminated scallops and phytoplankton obtained from Nova Scotia as well as from batch cultures of the dinoflagellate *Alexandrium ostefeldii*, isolated from the phytoplankton assemblages. Spirolides B **110** and D **111** were previously isolated from contaminated shellfish in the same area.[110] All of the spirolides display "fast-acting" toxicity in the traditional mouse bioassay due to the presence of a cyclic imine moiety. Spirolides

containing a vicinal dimethyl group in the seven-membered ring were found to be resistant to oxalic acid hydrolysis.[111] The relative stereochemistry of 13-desmethylspirolide C **109**, excepting that at one stereogenic centre, was determined from NMR data by application of the ConGen molecular modelling programme. 13-Desmethyl spirolide C **109** was found to have the same stereochemistry as pinnatoxins A[112,113] and D[114] in the regions of common structure. The relative stereochemistries of spirolides B **110** and D **111** were also partially determined by comparison of NMR data with those of 13-desmethyl spirolide C **109** and further use of ConGen.[115]

Spiro-prorocentrimine **112**, a novel macrocyclic lactone, was isolated from a culture of a benthic *Prorocentrum* sp. obtained from epiphytes of coral reef seaweeds in Taiwan. This lactone was much less toxic than other known marine cyclic imine toxins in the intraperitoneal mouse bioassay.[116] A new ester derivative of okadaic acid, DTX-6 **113** was isolated from a culture of a strain of *Prorocentrum lima*.[117] A culture of the marine diatom *Rhizosolenia setigera*, originally collected in France, was the source of highly branched isoprenoid pentaenes and hexaenes **114**-**117**.[118] Two galactopyranosyldiacylglycerols **118** and **119** were isolated from a cultured strain of the marine bacillariophycean microalga *Nitzschia* sp.[119]

## 3 Green algae

The depsipeptide kahalalide F **120**, isolated from the mollusc *Elysia rufescens* and from *Bryopsis* sp., the green algal food source,[120] has been synthesised.[121] HPLC, NMR spectroscopic and biological activity studies indicated that the stereochemistry proposed by Scheuer *et al.*[122] must be that of a less biologically active diastereomer. Four glycerol

derivatives, codiosides A-D **121**-**124** and a new derivative of *trans*-phytol, codioester **125** were isolated from an Arabian Sea collection of the green alga *Codium iyengarii*.[123]

## 4 Brown algae

The brown alga *Sargassum crispum* collected from the Red Sea was the source of sargassinone **126**.[124] The weakly cytotoxic (to P388 cells) hedaols A-C **127**-**129** were isolated from the Japanese brown alga *Sargassum* sp., and the absolute stereochemistry of hedaol A **127** established by the modified Mosher's method.[125] A dolabellane diterpene, hydroclathrol **130**, was isolated from the brown alga *Hydroclathrus tenuis*.[126] The first enantiospecific synthesis of (+)-cyclozonarone **131**, a sesquiterpene benzoquinone from the brown alga *Dictyopteris undulata*, has been achieved, utilising polygodial as starting material. The absolute configuration of the naturally occurring (–)-cyclozonarone was established as (5*R*,10*R*) by comparison of optical rotation and spectral data with those of (+)-cyclozonarone.[127] Four novel acyclic diterpenes **132**-**135** were isolated from the brown alga *Bifurcaria bifurcata* collected off the Atlantic coast of Morocco.[128] Two new aurones, 4'-chloro-2-hydroxyaurone **136** and 4'-chloroaurone **137** were isolated from *Spatoglossum variabile* collected off Karachi, Pakistan.[129] A synthesis of (all-*Z*)-henicosa-1,6,9,12,15,18-hexaene **138** starting from (all-Z)-icosa-5,8,11,14,17-pentaenoic acid (EPA) has been completed.[130] Compound **138** was originally isolated from the brown alga *Fucus vesiculosus*.[131]

## 5 Red algae

The red alga *Laurencia majuscula* collected from the South China Sea was the source of two compounds, the sesquiterpene 8-bromo-1-en-chamigrene **139** and a derivative of stigmastadiendiol **140**.[132] The first total synthesis of the *L. microcladia* metabolite (+)-rogioloxepane A **141**,[133] has been accomplished.[134] A total synthesis of (±)-aplysinal **142** from *Marginisporum aberrans*[135] has been carried out[136] and an asymmetric total synthesis of (–)-isolaurallene **143**, originally isolated from *L. nipponica yamada* has also been achieved.[137] *Laurencia pannosa* from Malaysia was the source of three novel antibacterial metabolites: pannosanol **144** and pannosane **145** are halogenated sesquiterpenes with an unusual rearranged chamigrene skeleton while (3*Z*)-chlorofucin **146** is a halogenated C15 acetogenin.[138] *L. luzonensis* from Okinawan waters yielded five bromosesquiterpenes, isopalisol **147**, luzonensol **148**, luzonensol acetate **149**, luzonensin **150** and (3*Z*,6*E*)-1-bromo-2-hydroxy-3,7,11-trimethyldodeca-3,6,10-triene **151** and a new bromoditerpene 3-bromobarekoxide **152**. X-ray analysis of **152** determined that the A/B and B/C ring junctions were both *trans*, in contrast to the *trans, cis* relative stereochemistry reported for the debrominated compound barekoxide, isolated from the sponge *Chelonaplysilla erecta*.[139] Reductive debromination of **152** and comparison of the NMR and optical data with those reported for barekoxide, confirmed that the absolute configuration of barekoxide is correctly represented as **153**.[140] Ma'iliohydrin **154**, a cytotoxic tribrominated chamigrene was isolated from a *Laurencia* sp. from the Philippines. Ma'iliohydrin exhibited cytotoxicity in the NCI 60-cell line human tumour screen and displayed especially potent activity against the NCI/ADR-RES breast cancer cell line.[141] *L. scoparia* collected in Brazilian waters was the source of four sesquiterpenes **155**-**158**. Scopariol **155** has a rearranged chamigrane skeleton while isorigidol **156**, is a β-chamigrene, as are the geometric isomers **157** and **158**.[142] An X-ray crystal structure of **156** established the absolute stereochemistry as (3*R*,6*S*,9*S*,10*S*).[143] An X-ray analysis of ma'ilione **159**, first isolated from *L. cartilaginea*[144] determined the absolute

stereochemistry as (6*S*,9*R*,10*S*).[142,143] Compound **156** and ma'ilione **159** exhibited moderate *in vitro* anthelmintic activity against the parasitant stage of *Nippostrongylus brasiliensis*.[142] Four squalene-derived triterpenes, martiriol **160**, pseudodehydrothyrsiferol **161**, dioxepandehydrothyrsiferol **162** and 16-epihydroxydehydrothyrsiferol **163** were isolated from *L. viridis* collected off the Canary Islands.[145] Calenzanol **164**, a sesquiterpene with a previously unreported ring system, was obtained as the major metabolite of *L. microcladia* off Elba Island in the Mediterranean. Calenzanol was found to be unstable, undergoing rearrangement at 40 °C to a novel indene.[146] Two halogenated C15 acetogenins, lembynes A **165** and B **166** were isolated from an unrecorded species of *Laurencia* collected in Malaysian waters. Lembyne A **165** displayed modest antibacterial activity against a range of marine bacteria.[147] *L. mariannensis* from Okinawa contained (12*E*)-lembyne A **167**. The halogenated sesquiterpene (6*R*,9*R*,10*S*)-10-bromo-9-hydroxy-chamigra-2,7(14)-diene **168** was isolated from *L. majuscula* from Okinawa and is the first report of this compound from a natural source. Both compounds **167** and **168** were active against a range of marine bacteria.[148] Prevezols A **169** and B **170** are brominated diterpenes isolated from *L. obtusa* from Greek waters.[149] A lanostanoid lactone, 5α-lanosta-8-en-3β,22ξ-dihydroxy-22(*R*),24(*S*)-lactone **171** was isolated from *Hypnea cerricornis* from the South China Sea.[150] The Taiwanese red alga *Ceratodictyon spongiosum* which contains the symbiotic sponge *Sigmadocia symbiotica* yielded the novel sterol *n*-nonadecanoic acid 24-methylenecholesteryl ester **172**.[151] Armatols A-F **173**-**178** are bromotriterpene polyethers isolated from an Indian Ocean collection of *Chondria armata*.[152] A Chilean collection of *Plocamium cartilagineum* yielded three tetrahydrofuran derivatives, furoplocamioids A-C **179**-**181**, which contain a chlorobromo vinyl moiety.[153] *P. cartilagineum* from the Mediterranean was the source of four polyhalogenated homosesquiterpenic acids **182**-**185**.[154] Two bromoditerpenes, sphaerolabdiene-3,14-diol **186** and bromosphaerone **187**, were isolated from a collection of

*Sphaerococcus coronopifolius* from the Atlantic coast of Morocco. Compound **187** exhibited antibacterial activity against *S. aureus*.[155]

## 6 Sponges

Once again, sponges have provided the greatest number of new marine natural products and have attracted considerable synthetic attention. An acetylated tetrahydroxyceramide **188** was isolated from an acetylated extract of *Fasciospongia cavernosa* collected on the South East coast of India.[156] Three sulfated ceramides, calyceramides A-C **189**-**191** with neuraminidase inhibition activity were obtained from a Japanese collection of *Discodermia calyx*.[157] A sponge of the genus *Calyx,* collected in Suluwasi, Indonesia, yielded a ketosphingolipid, calyxoside **192** with DNA-damaging properties.[158] The keto substitution of **192** was located by reductive amination of a penta-acetate derivative and analysis of MS fragmentation, while the relative and absolute stereochemistry was proposed from CD analysis of the perbenzoyl aglycone.[158] Three glycosphingolipids **193**-**195** were obtained from *Aplysinella rhax* collected in New Caledonia.[159] A presumably new species of *Haliclona* from Queensland contained four unsaturated aminoalcohols **196**-**199** with antifungal properties.[160] (2*S*,3*R*,11*S*,12*R*,2'''*R*,11'''*S*,12'''*R*)-Plakoside A **200** was synthesised[161,162] and found to have optical rotation and spectroscopic data identical to plakoside A from *Plakortis simplex*.[163] The spectroscopic data were also identical to the previously synthesised (2*S*,3*R*,11*R*,12*S*,2'''*R*,11'''*R*,12'''*S*) diastereomer **201**; the absolute stereochemistry of the cyclopropyl groups remains unknown.

Three furan-containing fatty acid derivatives, plakorsins A-C **202**-**204**, and an epoxide, plakortic acid **205** were isolated from Taiwanese *P. simplex* specimens.[164] The sponge *Spirastrella abata* collected from Korean waters yielded four phosphatidylcholines

**206**-**209** of which **208** and **209** showed an inhibitory effect on the biosynthesis of cholesterol.[165] *Callyspongia fallax* collected in the Caribbean was found to contain the methoxylated acids **210**-**215**.[166] Two antimicrobial lysoplasmanylinositols **216**-**217** were isolated from a Japanese *Theonella swinhoei*.[167] (–)-Halicholactone **218** from *Halichondria okadai*[168] was synthesised stereoselectively using chiral (diene)$Fe(CO)_3$ complexes.[169] Three dithiocyanates, thiocyanatins A **219**, B **220**, and C **221**, were isolated from an *Oceanapia* species collected from South West Australia. These compounds have nematocidal activity and their structures were confirmed by synthesis.[170] *Acarnus bicladotylota* collected from the South West coast of India yielded the acetylenic cycloperoxides, peroxyacarnoic acids C **222** and D **223** which were isolated as their methyl esters.[171] A further series of cytotoxic polyacetylenic alcohols **224-236**, have been isolated from a Korean *Petrosia* species that has previously yielded similar compounds.[172,173] The absolute stereochemistry of (–)-adociacetylene B **237** from *Adocia* sp.[174] was confirmed from a synthesis of both (+) and (–) isomers employing enzymatic resolution.[175]

The amphiasterins A1-4 **238**-**241**, B1-5 **242**-**246**, C1-4 **247**-**250**, D1-3 **251**-**253** and E1 **254** have been isolated from *Plakortis quasiamphiaster* collected in Vanuatu.[176] The magnesium salt of the previously reported ancorinoside A, isolated from an *Ancorina* species, has been reported as a new compound.[177] Three ancorinosides, B **255**, C **256** and D **257**, isolated from a Japanese collection of *Penares sollasi*, were found to be inhibitors of membrane type 1 matrix metalloproteinase.[178] The moderately antifungal plakinic acid F **258** and epiplakinic acid F **259** together with plakortolide F **260** were obtained from a *Plakinastrella* species collected in the Seychelles.[179] The name plakortolide F was also given to a different peroxide lactone **261** which was isolated along with plakortolide G **262** from a Jamaican *Plakinastrella onkodes* collection. The absolute stereochemistry of **262** was proposed from a combination of optical rotation and molecular modelling data.[180] The

cytotoxic methyl capucinoate A **263** and the related compound **264** were isolated from a Dominican collection of *P. onkodes*;[181] a structure with the same gross connectivity was reported earlier at a conference.[182] In the same paper the isolation of glanvillic acid A **265** and B **266** from a Dominican *Plakortis halichondrioides* was also reported. The compounds were separated and characterised as the methyl esters.[181] An Okinawan specimen of *P. lita* yielded two further cyclic peroxide acids, the haterumadioxins A **267** and B **268** with moderate cytotoxicity.[183] Four further plakortides, I-L **269**-**272** were reported from an undescribed species of *Plakortis* collected in Jamaica.[184] A γ-lactone, plakortone G **273**, mildly active against *Plasmodium falciparum*, was isolated from an apparently different undescribed Jamaican *Plakortis* species.[185]

The absolute stereochemistries of the salicylihalamides A **274** and B **275** from *Haliclona* sp.[186] have been revised following a re-interpretation of Mosher ester derivatives[187] and enantioselective syntheses of both enantiomers of each.[188,189,190] Two hydroxypyranones **276** and **277** were obtained from the Thai sponge *Tetilla japonica*.[191] Onnamide F **278**, isolated from the South Australian sponge *Trachycladus laevispirulifer*, was found to be a potent nematocide.[192] A further six bengamides **279**-**284** with varying *in vitro* antitumour activity were obtained from Fijian collections of *Japsis* cf *coriacea*.[193]

A Vanuatuan specimen of the genus *Spongia* was found to contain a cytotoxic macrolide spongidepsin **285**,[194] while the cytotoxic macrolide, dactylolide **286**, was found in a Vanuatuan sponge of the genus *Dactylospongia*.[195] The enantioselective synthesis of (+)-zampanolide[196] has established the absolute and relative stereochemistry of the (–) antipode **287** isolated from *Fasciospongia rimosa*.[197] Three further, potently cytotoxic, chondropsin macrolide lactams were reported from three different sponges: 73-deoxychondropsin A **288** was isolated from an Australian *Ircinia ramosa*, chondropsin C **289** was found in a Philippine *Ircinia* species,[198] while an Australian *Chondropsis* species yielded chondropsin D **290**.[199] A

Vanuatuan specimen of the genus *Haliclona* was found to contain the *in vitro* antitumour macrolide halicamide **291**.[200]

The weakly cytotoxic heptapeptide, wainunuamide **292** was isolated from *Stylotella aurantium* collected in Fiji.[201] The total synthesis of *cis,cis*-ceratospongamide **293** from the red alga *Ceratodictyon spongiosum* and symbiotic sponge *Sigmadocia symbiotica*[202] has been reported.[203] Hymenamide C **294** from *Hymeniacidon* sp.[204] has been synthesised using solid support methodology.[205] A total synthesis of phakellistatin 11 **295**, isolated from *Phakellia* sp.,[206] revealed that the synthetic product is much less cytotoxic than the originally isolated sample.[207] A collection of *Sidonops microspinosa* from Sulawesi, Indonesia was found to contain the HIV-inhibitory depsipeptide microspinosamide **296**.[208] The structures of two potent anti-inflammatory peptides, halipeptin A **297** and B **298**, isolated from a member of the genus *Haliclona* from Vanuatu, were proposed from an analysis of spectroscopic data.[209] Two iron-chelating peptides, haliclonamide A and B, isolated from a *Haliclona* species collected in Palau were proposed to have structures **299** and **300** respectively on the basis of spectroscopic analysis.[210]

A potent, neurologically-active amino acid, neodysiherbaine A **301** has been reported as a minor metabolite of a Micronesian *Dysidea herbacea*. The relative and absolute stereochemistries were determined by asymmetric total synthesis.[211] The enantioselective synthesis of both (+)- and (–)-dysibetaine **302**, isolated from *D. herbacea*,[212] has established the absolute configuration as (*S*,*S*).[213] Two polychlorinated thiazoles **303** and **304** were isolated from Queensland specimens of *D. herbacea*.[214] From the same collection, several polychlorinated dipeptides **305**-**309** were reported separately; the absolute stereochemistries were determined by comparison of optical rotation data.[215] The methyl esters **305**-**307** are considered to be artifacts of methanolic extraction. An undescribed species of *Dysidea*

collected in the Philippines yielded the proline-derived dysideaprolines A-F **310**-**315** together with the enol-ether containing barbaleucamides A **316** and B **317**.[216]

Two antifungal bromopyrroles, 3-bromomaleimide **318** and 3,4-dibromomaleimide **319**, were found in *Axinella brevistyla* collected in Japan.[217] (–)-Haliclorensin, isolated from *Haliclona tulearensis*,[218] and assigned the structure **320**, was synthesised by two independent groups and found to be spectroscopically non-identical with the natural product.[219,220] Subsequently, a re-isolation and re-investigation of the spectroscopic data led to a revised structure **321** that was confirmed by enantioselective synthesis of both enantiomers.[221] Both enantiomers of stellettadine A **322** from *Stelletta* sp.[222] were synthesised from (*S*)- and (*R*)-citronellal.[223,224] The (*S)* isomer was found to have a negative rotation similar to the natural compound which had previously been assigned as (*R*).[223] (–)-Stellattamide B, originally reported from a *Stelletta* sp. with a (6''*S*) configuration,[225] has now been established as (1*S*,4*S*,8a*R*,6''*R*) **323** by total synthesis.[226] (+)-Batzelladine F, originally isolated from *Batzella* sp.,[227] recently re-assigned as *Monanchora arbuscula*,[228] was originally assigned structure **324**. The structure has been revised to **325** on the basis of the enantioselective synthesis of both the revised and putative structures.[229] Mirabilin G **326** was isolated from a South Australian *Clathria* species.[230] The Palauan sponge *Protophlitaspongia aga* yielded 3,4,5,6-tetrahydro-6-hydroxymethyl-3,6,dimethyl-4-pyrimidinecarboxylic acid **327** that was found to inhibit the settling of larvae of the barnacle *Balanus amphitrite*.[231] The wondonins A **328** and B **329** were isolated from an association of *Poecillastra wondoensis* and a *Japsis* species from Korea.[232] Naamine B **330** from *Leucetta chagosensis*[233] has been synthesised.[234]

*Hyrtios erecta* collected in Okinawa yielded two selective inhibitors of neuronal nitric oxide synthase **331** and **332**.[235] An asymmetric synthesis of (+)-chelonin B **333** from *Chelonaplysilla* sp.[236] employing a Sharpless asymmetric dihydroxylation established the stereogenic centre as (*S*).[237] The synthesis of the (–) enantiomer of (+)-hamacanthin A **334**

isolated from *Hamacantha* sp.[238] established the stereogenic centre as (*S*).[239] Xestomanzamine B **335** from *Xestospongia* sp.[240] was synthesised via a Pictet-Spengler condensation of tryptamine with a vicinal tricarbonyl substituted imidazole.[241] A manzamine dimer, *neo*-kauluamine **336**, was isolated from an undescribed genus of the family Petrosidiidae collected from Sulawesi, Indonesia along with the antipodes of 8-hydroxymanzamine **337** and manzamine F **338.** These antipodes were found to have potent *in vivo* activity against *Plasmodium berghei*.[242] The manzamines have been isolated from a variety of sponge genera from various orders. The authors speculate that some of these sponges may be members of this new genus of the Petrosidiidae family.[242]

A revised structure **339** for pyrinodemin A **340** from *Amphimedon* sp.[243] has been proposed from spectral comparison of the natural product to the synthesised structures.[244] Pyrinodemin B **341** from the same sponge[245] was also synthesised.[244] Variolin B **342** from *Kirkpatrickia varialosa*[246] was synthesised via a tandem deoxygenation and cyclisation of a triarylmethanol intermediate.[247] Two bromoquinolones **343** and **344** were isolated from Okinawan specimens of *Hyrtios erecta*: **343** is a known synthetic compound.[235] A *Haliclona* species from the Philippines contained 1-hydroxymethyl-7-methoxyisoquinolin-6-ol **345**.[248] The structure of renieramycin H, previously described from *Haliclona cribricutis* as **346**[249] has been re-assigned as **347** on the basis of spectral comparison to synthetic model compounds.[250] Subsequently, it was found that this structure was assigned to cribrostatin 4 on the basis of X-ray analysis.[251] The NMR spectra of the two compounds were found to be identical, and accordingly, the trivial name renieramycin H must be given to this structure. Makaluvamine P **348**, with cytotoxic and antioxidant activity, was isolated from the Vanuatuan sponge *Zyzzya* cf. *fuliginosa*.[252] Two *Xestospongia* species collected in Palau and the Philippines contained the DNA-cleaving agent deoxyamphimedine **349**.[253]

The absolute stereochemistry of (*R*)-(–)-axinellamine **350**, isolated from *Axinella* sp.[254] was determined by synthesis of the (*S*) isomer.[255] The enantiomers of (+)-slagenin B **351** and (–)-slagenin C **352** from *Agelas nakamurai*[256] were synthesised stereospecifically, establishing the absolute stereochemistry as (9*R*, 11*R*, 15*R*) and (9*R*, 11*S*, 15*S*) respectively.[257] A total synthesis of phorbazole C **353** from *Phorbas* aff. *clathrata*[258] was achieved with the central oxazole ring formed by cyclodehydration of an acylaminoketone.[259] The *N*-methyl oroidin derivative, sventrin **354**, reported from the Bahaman sponge *Agelas sventres*, was found to be a feeding deterrent to the reef fish *Thalassoma bifasciatum*.[260] *Axinella carteri* from the Philippines afforded ugibohlin **355**, a dibromopyrrole derivative.[261] *A. brevistyla* from Japan was found to contain 12-chloro-11-hydroxyldibromoisophakellin **356** and *N*-methylmanzacidin C **357**. Both displayed antifungal and cytotoxic activity.[217] *N*-Methyldibromoisophakellin **358**, isolated from the Bahaman sponge *Stylissa caribica*, was found to inhibit the feeding of the reef fish *T. bifasciatum*.[262]

The weakly cytotoxic methoxypurine, mucronatine **359**, was isolated from the French Mediterranean sponge *Stryphnus mucronatus*.[263] *Zyzzya fuliginosa* from the Philippines afforded 3,7-dimethylguanine **360**.[264] A weak inhibitor of CDC2 kinase, microxine **361**, a taurine-bearing purine derivative, was isolated from an Australian *Microxina* species.[265]

Purealidin N **362** from *Psammaplysilla purea*[266] was synthesised with the oxime formed from addition of hydroxylamine chloride to a silyl-enol ether.[267] Inhibitors of the novel mycobacterial enzyme mycothiol S-conjugate amidase, the bromotyrosine-derived alkaloids **363** and **364**, were isolated from an Australian *Oceanapia* species; the absolute stereochemistry of **363** was determined by comparison of the optical rotation to similar compounds.[268] *Pseudoceratina purpurea* collected in Okinawa contained zamamistatin **365**, a growth inhibitor of the adherent bacterium *Rhodospirillum salexigens*. The absolute stereochemistry was determined by analysis of the Mosher's acid derivatives.[269] Aplyzanzine

A **366** was reported from an *Aplysina* species collected near Zanzibar.[270] A *Suberea* species from Okinawa yielded the cytotoxic suberedamines A **367** and B **368**. Chemical degradation to (*S*)-tyrosine allowed assignment of the absolute configurations.[271] Archerine **369**, isolated from the Caribbean sponge *Aplysina archeri*, displayed antihistamine activity in isolated guinea pig ileum.[272] The tokaradines A **370**, B **371** and C **372**, isolated from *Pseudoceratina purpurea* collected in southern Japan, were found to be toxic to the crab *Hemigrapsus sanguineus*.[273] *Suberea* aff. *praetensa*, collected in Thailand, yielded 11,17-dideoxyagelorin A **373** and B **374**.[274]

Four polybrominated phenols **375**-**378** were isolated from *Phyllospongia dendyi* collected in Palau. These compounds were found to be toxic to a variety of micro- and macro-algae.[275] *Dysidea dendyi* collected from the North West coast of Australia yielded two tetrabrominated dibenzo-*p*-dioxins, spongiadioxins A **379** and B **380**.[276] Iantheran B **381**, isolated from an *Ianthella* species collected from the Great Barrier Reef, Australia was found to be a Na/K-ATPase inhibitor.[277]

The merosesquiterpenoids hippochromin A **382** and B **383** were isolated as acetates from a Taiwanese specimen of *Hippospongia metachromia*.[278] Two rearranged merosesquiterpenoids dysidenone A **384** and B **385** and the related selective $PLA_2$ inhibitor, dysidine **386** were isolated from a sponge of the genus *Dysidea* collected in Vanuatu.[279] Dactyloquinones A **387** and B **388** were reported from a *Dactylospongia elegans* specimen collected in Okinawa.[280] Smenospondiol **389** from a *Smenospongia* sp.,[281] also known as dictyoceratin A from *Hippospongia* sp.[282] was synthesised by titanium-mediated tandem radical cyclisation as a racemic mixture.[283] Two racemic and one asymmetric syntheses were reported for (+)-frondosin B **390**, isolated from *Dysidea frondosa,*[284] establishing the configuration of the stereogenic centre as (*R*).[285] A diterpene-4-hydroxybenzoic acid derivative, subersic acid **391**, with human lipoxygenase inhibitory activity was isolated from

a Papua New Guinean *Suberea* species together with a diterpene described below.[286] The hipposulfates A **392** and B **393**, isolated from an Okinawan *Hippospongia* cf. *metachromia*, were found to have moderate cytotoxicity.[287] The New Caledonian sponge *Coscinoderma mathewsi* afforded the CDC25 phosphatase inhibitor (+)-coscinosulfate **394** along with an unnamed congener **395**.[288] The relative and absolute stereochemistry of **394** was confirmed by total asymmetric synthesis.[289] Interestingly, halisulfate 1, previously isolated from a *Halichondria* sp.,[290] was reported with the same relative stereochemistry. Halisulfate 1 has a reported optical rotation of –27.3° while that of coscinosulfate is +5°; differences in $^{1}$H-$^{1}$H coupling constants near the sulfate groups were noted,[288] but unfortunately the NMR solvent used was different in the two studies.

The sequiterpenoid furodysin lactone **396** and a related amino acid derivative, pyrodysinoic acid **397**, were obtained from a blue/grey encrusting member of the genus *Dysidea* collected from the Philippines.[291] A specimen of *Dysidea herbacea* collected from Lizard Island, Australia was found to contain 6-hydroxyfurodysinin **398**.[214] Three carbonimidic dichlorides, **399**-**401**, and two related α,β unsaturated aldehydes **402** and **403**, were isolated from *Sylotella aurantium* collected from Okinawan waters.[292] The North Queensland sponge *Ulosa spongia* also contained **401** along with the related diol **404**.[293] Two enantiomeric syntheses of (+)-kelsoene **405** from *Cymbastela hooperi*[294] have established the absolute stereochemistry.[295,296]

Three weakly cyctotoxic C19 norditerpene peroxides, aikupikoxides B **406**, C **407**, and D **408** were isolated from *Diacarnus erythraenus* collected from the Red Sea along with a related norsesterterpenoid discussed below.[297] The hamigerans **409**-**412**, isolated from *Hamigera tarangaensis*[298] were synthesised via an intramolecular Diels-Alder trapping of a photochemically generated hydroxy-*o*-quinodimethane.[299] (+)-Subersin **413** was isolated from a Papua New Guinean *Suberea* species.[286] The absolute stereochemistry was proposed by

comparison of its optical rotation to that of a similar structure. The structure of cacospongin A, isolated from a Philippine sponge of the genus *Cacospongia*, has been re-assigned to the same diterpene skeleton with no stereochemistry specified.[300] The $^{13}C$ and $^{1}H$ NMR data are identical to that of **413** but the sign of the optical rotation is opposite, suggesting an enantiomeric relationship. *Spongia zimocca* subspecies *irregularia* from China yielded the norditerpenoid zimoclactone B **414** and the diterpenoid zimoclactone C **415**.[301] A South Australian species of *Phorbas* yielded phorbasin B **416** and its acetate, phorbasin C **417**.[302] A quite remarkable cumulated ketene containing compound, irciniketene **418** with moderate cytotoxicity, has been reported from *Ircinia selaginea* collected in Guangxi Province, China.[303] A *Cacospongia* species collected in Okinawa contained (–)-cacofuran A **419** and the acetate, cacofuran B **420**. The absolute stereochemistry was determined from an analysis of the MPTA esters of **419**.[304] It was noted that both compounds inhibited the development of fertilised sea urchin eggs. The tricarbocyclic epipolone **421** and epipolol **422** were obtained from *Epipolasis reiswigi* collected in Puerto Rico.[305]

The C21 norsesterterpenoid originally reported with conjugated double bonds **423**[306] has been revised to **424** on the basis of more complete spectroscopic data obtained from a sample isolated from an Australian specimen of *Spirastrella papilosa*.[307] The absolute stereochemistry was determined by degradation and the name (–)-isotetrahydrofurospongin-1 is proposed for this bisfuranoterpene. Two unusual trisnorsesterterpenoid lactams, the sarcotragins A **425** and B **426** were isolated from a *Sarcotragus* species from Jaeju Island in Korean waters.[308] Five cyctotoxic furanosesterterpenoids, the sacotins A-E, **427**-**431** were reported from a different specimen of *Sarcotragus* sp. collected at Cheju Island, Korea.[309] The absolute stereochemistries of **429**-**431** were determined by comparison of CD spectra. The Red Sea sponge *Diacarnus erythraenus* was found to contain the antiviral and cytotoxic C24 norstesterterpenoid muqubilone (aikupikoxide) **432** by two independent groups.[310,297] (–)-

Idiadione **433** from *Spongia idia*[311] was synthesised from (–)-citronellal, establishing the stereogenic centre as (*S*).[312] A Palauan species of *Thorectandra* yielded the cytotoxic thorectandrols A **434** and B **435**.[313] The cytotoxic kohamaic acids A **436** and B **437** were isolated from an *Ircinia* species from Okinawa.[314] Three tricarbocyclic sesterterpenoids **438**-**440** of the cheilanthane class isolated from a Queensland *Ircinia* sp. were found to be inhibitors of MSK1 and MAPKAPK-2 protein kinases.[315] Five inhibitors of *in vitro* HIV-1 envelope-mediated fusion, the phyllolactones A-E **441**-**445**, were obtained from specimens of *Phyllospongia lamellosa*.[316]

A undescribed species of *Gellius* from the Caribbean coast of Panama yielded four acetylenic sterols, gelliusterol A-D **446**-**449**; gelliusterols A, B and C were found to be moderately cytotoxic.[317] Stigmast-5-ene-7-one-3β-ol **450** was obtained from *Polymastia sobustia* from the South China Sea.[318] A cytotoxic and apoptosis-inducing rearranged sterol, orostanal **451** was obtained from *Stelletta hiwasaensis* collected in Japan.[319] The 6-5-6-5 fused ring system has only been found previously in the terrestrial plant *Taiwania cryptomeriodes*;[320] the absolute stereochemistry of **451** was established from analysis of the CD spectrum. A South China Sea specimen of *Geodia japonica* yielded 26-methylergosta-5,24(28)-dien-3β-ol **452** along with several nortriterpenoids discussed below.[321] Two steroidal alkaloids, plakinamine E **453** and F **454** exhibiting moderate cytotoxicity, antifungal activity and nucleic acid-cleaving properties, were isolated from an undescribed species of *Corticium* collected at Guam.[322] A sulfated sterol ester, clathsterol **455** with anti-HIV-1 reverse transcriptase activity was obtained from an Eritrean sponge of the genus *Clathria*.[323] Two phosphorylated sterol sulfates **456** and **457**, isolated from a *Cribrochilina* species collected from Japan were found to be inhibitors of membrane-type matrix metalloproteinase.[324] The absolute stereochemistry of **456** was determined by Mosher's method and was found to be identical to haplosamate A **458** from two haplosclerid sponges[325]

leading to a structural revision of **456** and that of haplosamate B to **459**. A Philippine sponge of the genus *Xestospongia* contained two sulfated sterols, ibisterol B **460** and C **461** and an epoxysteroid **462** that were found to be inhibitors of HIV-1 integrase.[326] (+)-Agosterol A **463** from *Spongia* sp.[327] was synthesised from ergosterol.[328] The unusual 15-keto steroid, xestobergsterol **464** from *Xestospongia bergquisti*[329] has been synthesised from stigmasterol.[330]

Two nortriterpenes of the isomalabaricane class, geoditins A **465** and B **466** were isolated from *Geodia japonica* from the South China Sea.[321] A *Japsis* species collected near Tonga yielded three cytotoxic isomalabaricanes, 29-hydroxystelliferin E **467**, 29-hydroxystelliferin A **468** and stelliferin G **469**.[331] The glycosylated triterpenoid, stelliferin riboside **470**, was obtained from a Fijian collection of *G. globostellifera*.[332] In an extensive re-investigation of two populations of the Red Sea Sponge *Siphonochalina siphonella*, sipholenols G **471**, F **472** and H **473**, sipholenone D **474**, sipholenoside A **475** and B **476**, siphonellinol B **477**, neviotine B **478** and dahabinone A **479** were isolated.[333] The relative concentrations of these and previously described triterpenoids were compared between the two populations. An *N*-acetyl aminoglycoside, formoside B **480**, isolated from the Caribbean sponge *Erylus formosus* was found to be an anti-feedant against the ecologically relevant reef fish *Thalassoma bifasciatum*.[334] The moderately cytotoxic *N*-acetyl aminoglycosides, erylosides G-J **481**-**484** were obtained from Korean specimens of *Erylus nobilis*.[335] A Caribbean sponge, *Ectyoplasia ferox*, afforded the norlanostane glycosides feroxosides A **485** and B **486**.[336] A bacteriohopanoid, (32*R*,33*S*,34*S*)-32,35-anhydrobacteriohopanetetrol **487** was isolated in significant quantities (0.2% dry weight) from the Bahaman sponge *Plakortis simplex*.[337] A compound having the structure proposed for hippospongic acid A **488**, isolated from *Hippospongia* sp.,[338] was synthesised by two independent groups.[339,340] It was noted, however, that the spectral details of the synthetic product did not match the natural

compound, and a revised structure for (+)-hippospongic acid A **489** was proposed and confirmed by enantioselective total synthesis.[339]

A Caribbean collection of *P. simplex* contained the heptaisoprenylhexasaccharide, plaxyloside **490**. Isolation and structural elucidation were performed on the peracetate.[341]

## 7 Coelenterates

The chemistry of the coelenterates continues to be predominantly terpenoid or steroid in nature. The structure and absolute stereochemistry of eunicenone A **491**, a tetraprenylated cyclohexenone metabolite isolated from the gorgonian *Eunicea* sp.,[342] has been confirmed by total synthesis.[343] In two separate accounts, eight briarane skeleton diterpenoids briaexcavatolides K-N **492**-**495**[344] and O-R **496**-**499**[345] were isolated from the gorgonian *Briareum excavatum*. Relative stereochemistry was secured by X-ray analysis for **492**, **496** and **497**. In a separate study, the same organism contained the diterpenes, briantheins A-C **500**-**502**.[346] The relative stereochemistry of **500** was established by NOESY NMR experiments and the preparation of MTPA esters helped establish the absolute stereochemistry. Brianthein A **500** reversed MDR in a human carcinoma cell line. A Western Pacific collection of the gorgonian *B. stechei* contained eleven briarane diterpenes, the milolides **503**-**513** and several known metabolites.[347] A consequence of the NMR assignments of **503**-**513** was the revision of the relative stereochemistry of solenolide C **514**,[348] also isolated from the organism. New examples of xenicane diterpenes acalycixeniolides H-L **515**-**519**, were isolated as cytotoxic components of the gorgonian *Acalycigorgia inermis*.[349] The mildly cytotoxic acyclic sesquiterpenes and norsesquiterpenes **520**-**526** were isolated from the Caribbean gorgonian *Plexaurella grisea*.[350] The structure and absolute stereochemistry of (–)-astrogorgiadiol **527**, isolated from the gorgonian *Astrogorgia* sp.,[351] has been secured by

total synthesis.[352] Thirteen polyoxygenated sterols **528**-**540** were isolated from an Indonesian collection of the gorgonian *Isis hippuris*.[353] Of the compounds tested, spiroketal-containing sterol **528** exhibited the most potent cytotoxicity. A Taiwanese collection of *I. hippuris* contained two polyhydroxylated sterols isihippurols A **541** and B **542**, as well as nine known sterols.[354] The gorgonian *Euplexaura anastomosans* contained two farnesylhydroquinone derivatives euplexides F **543** and G **544**.[355] Both metabolites exhibited mild cytotoxicity and inhibited $PLA_2$. Two antimycobacterial diterpenes and a bisditerpenoid **545**-**547** were isolated from the sea whip *Pseudopterogorgia elisabethae*.[356] A racemic synthesis of colombiasin A **548**, also isolated from *P. elisabethae*,[357] has been reported.[358] An Indian Ocean collection of the gorgonian *Pseudopterogorgia* sp. contained the antibacterial ceramide derivative **549**.[359] The structure reported for the antimycobacterial diterpene pseudopteroxazole **550**[360] and its C-1 diastereomer **551** have been synthesised but neither have the same spectroscopic data as the natural product.[361] The revised structure of pseudopteroxazole was proposed to be **552**. Examination of the Caribbean gorgonian *Eunicea* sp.[362] afforded two cembrane glycosides, calyculaglycosides D **553** and E **554**, and the (+)-antipode of the known cembrane nephthenol **555**.[363] Chemical conversions and closer comparison with the spectroscopic data observed for **553** and **554** required revision of the previously published structures of calyculaglycosides A-C[364] to **556**-**558**. The Caribbean gorgonian *Plexaurella grisea* contained six sterols **559**-**564** and several known compounds.[365] Many of the sterols exhibited *in vitro* antitumour activity towards the HT-29 cell-line. A mildly cytotoxic sesquiterpene, junceol A **565**, was isolated from the sea pen *Virgularia juncea*.[366] Briarane skeleton terpenoids, cavernulin A **566** and B **567** were isolated from a *Cavernularia* sp.[367] A metabolite containing an aromadendrane-type skeleton, 3-acetoxyspathulenol **568**, was isolated from the soft coral *Parerythropodium fulvum*.[368] Paesslerins A **569** and B **570**, the first examples of metabolites containing the 2,8,8,10-tetramethyltricyclo4.3.2.$0^{2,5}$undecane (paesslerane) skeleton, were isolated from a

South Georgia Island collection of the pink soft coral *Alcyonium paessleri*.[369] The structure of the cytotoxic sterol **571**, isolated from *A. patagonicum*,[370] has been confirmed by total synthesis.[371] The diterpenes pachyclavulariaenones A-C **572**-**574** were isolated from the soft coral *Pachyclavularia violacea*.[372] The structure and relative stereochemistry of **574** was confirmed by X-ray analysis. Seven diterpenes, pachyclavulariolodes G-L **575**-**580**, and secopachyclavulariaenone A **581**, and the two known analogues pachyclavulariolide **582**[373] and pachyclavulariolide E **583**[374] were also reported from *P. violacea*.[375] The structures of **575**, **576**, **582** and **583** were secured by X-ray analysis. Several accounts of the total synthesis of the revised structure of sclerophytin A **584**,[376,377] cladiell-11-ene-3,6,7-triol **585**[378] and 6-acetoxycladiell-7(16),11-dien-3-ol **586**[379] have been reported.[380,381,382] Two diterpenes caribaeorane **587** and 15-hydroxycaribaeorane **588** were isolated from the soft coral *Erythropodium caribaeorum* as their C-4 methylketals **589** and **590**.[383] The observation of facile ketal formation suggests that the C-4 methylketal contained in the antimitotic drug lead eleutherobin **591**[384] is an artifact of isolation. In addition to three known diterpenes that included 2-hydroxynephthenol **592**,[385] three norditerpenes, chabrolols A-C **593**-**595** were isolated from the soft coral *Nephthea chabroli*.[386] X-ray analysis of **592**-**595** secured the respective relative stereochemistries. Six dolabellane diterpenes **596**-**601** have been isolated as the cytotoxic components of the Formosan soft coral *Clavularia inflata*.[387] An Okinawan collection of *C. viridis* contained three chlorinated steroids, yonarasterols G, H, and I **602**-**604**.[388] The absolute stereochemistry of **603** was equated with the stereochemically-defined analogue stoloniferone-c[389] by chemical conversion. In a separate study, five halogenated prostanoids **605**-**609** were obtained from *C. viridis*.[390] Absolute stereochemistries were assigned based upon chemical conversion and the modified Mosher's method for **605** and by subsequent comparison of CD data for **606**-**609**. Eight sesquiterpenes, tubipolides A-G **610**-**616** and tubiporone **617** were isolated as mildly cytotoxic components of the Formosan

stolonifer *Tubipora musica*.[391] Specimens of the soft coral *Cladiella* sp. collected from Andaman and Nicobar Islands contained the sterol **618** and glycolipid **619**,[392] while an Andaman Island collection of the same genus contained a mixture of cerebroside homologues **620**.[393] The soft coral *Sinularia dissecta* yielded the sesquiterpene **621**.[394] Absolute stereochemistry of **621** was deduced from interpretation of CD data and by preparation of MTPA esters. The soft corals *Sarcophyton trocheliophorum* and *Lithophyton arboreum*, collected in the Red Sea, contained six novel fatty acid derivatives **622**-**627**.[395] The structure and absolute stereochemistry of (–)-13-hydroxy-11,12-epoxy-neocembrene **628**, also isolated from *S. trocheliophorum*,[396] has been secured by total synthesis.[397] The soft coral *S. molle* contained the known diterpene lactone sarcophinone **629**[398] and the new diastereomer iso-sarcophinone **630**.[399] Both compounds exhibited *in vitro* antitumour activity. Two cembrene alcohols, one new, acutanol **631** and one known, sarcophytol A **632**,[400] have been reported from the soft coral *S. acutangulum*.[401] The absolute configuration of **632** was confirmed by the preparation of the NMA ester. A polyhydroxylated sterol sardisterol **633** was isolated from the soft coral *S. digitatum.*[402] The structure and absolute configuration of stolonidiol **634**, isolated from the soft coral *Clavularia* sp.,[403] was established by total synthesis.[404] Pyridinium alkaloids are predominantly the preserve of sponges. However, a new pyridinium alkaloid, montipyridine **635**, has been reported from the stony coral *Montipora* sp.[405] Also isolated from the same genus were a range of cytotoxic diacetylenes **636**-**645**.[406] Absence of optical activity for **641**-**643** and the formation of diastereomeric mixtures of MTPA esters suggested that **641**-**643** were isolated as racemic mixtures. A crystal structure to 1.9 Å resolution was reported for the pore-forming toxin equinatoxin II (EqtII) purified from the sea anemone *Actinia equina*.[407] Two polypeptide toxins, RSAP I and II, of molecular masses 5008 and 4992 Da respectively, have been purified from the sea anemone *Actinia ceri*.[408]

## 8 Bryozoans

Despite their history of yielding novel natural products, there continues to be very little new work reported on bryozoan metabolites, although some syntheses have been carried out. Total syntheses of the *Flustra foliacea* metabolites flustramine A **646**[409] and flustramides A **647**[410] and B **648**[411] have been accomplished[412] and the first synthesis of (–)-debromoflustramine B **649**, also from *F. foliacea,*[413] has been achieved.[414]

## 9 Molluscs

The relative and absolute stereochemistry of (–)-membrenone C **650**, isolated from *Pleurobranchus membranaceus*,[415] has been secured by synthesis.[416] Several accounts of stereoselective syntheses of (+)-testudinariols A **651** and B **652**, ichthyotoxic metabolites from *P. testudinarius*,[417] have been reported.[418,419,420] Aplydactone **653**, a structurally unprecedented sesquiterpene was isolated from the sea hare *Aplysia dactylomela*.[421] The absolute stereochemistry of the metabolite was established by X-ray analysis. The complete $^{1}$H and $^{13}$C NMR assignments of the *A. dactilomela* [sic] metabolites johnstonol **654**, pacifenediol **655**, pacifidiene **656**, and pacifenol **657** have been reported.[422] Two tryptophan-derived dipeptides **658** and **659** were isolated from a New Zealand collection of the sea hare *A. dactylomela*.[423] The absolute stereochemistry of **658** was determined by synthesis of deoxo-diastereomers and comparison of CD spectra. A novel glycosphingolipid, EGL-II **660** has been isolated from eggs of the sea hare *A. kurodai*.[424] The stereochemistry of (–)-aplyolide A **661**, an ichthyotoxic metabolite from *A. depilans*,[425] has been confirmed by synthesis.[426] A Japanese collection of the sea hare *Dolabella auricularia* contained auriculol **662**, a novel cytotoxic squalene metabolite.[427] The structure and absolute stereochemistry was

confirmed by synthesis. Fourteen drimane sesquiterpenes, dendocarbins A-N **663**-**676** were isolated from the nudibranch *Dendrodoris carbunculosa*.[428] The ethoxy groups present in **671**, **672** and **674** suggest that these compounds are probably artifacts of the use of ethanol to extract the organism. Compound **672** exhibited cytotoxicity towards MDR tumour cell lines. The relative and absolute stereochemistry of (+)-shahamin K **677**, which was isolated from *Chromodoris gleneii*,[429] has been confirmed by synthesis.[430] Nine metabolites **678**-**686** were identified in chemical studies of the South African nudibranch *Leminda millecra*.[431] GC-MS analysis of potential octacoral prey species identified two likely dietary sources for some of the metabolites, including **679**. Attenols A **687** and B **688**, cytotoxic spiro-acetals isolated from the Chinese bivalve *Pinna attenuata*,[432] have been synthesised enantioselectively.[433] A novel shell fish-derived chlorosulfolipid toxin **689** was isolated from *Mytilus galloprovincialis*.[434] The absolute stereochemistry of **689** was determined by a combination of molecular modelling and Mosher's methodology. From the digestive glands of the same species were isolated three bioactive alkaloids, oxazinins 1-3 **690**-**692**.[435] The absolute stereochemistry of oxazinin-1 **690** was subsequently secured by derivatisation and NMR analysis.[436] Pinnatoxins B **693** and C **694**, isolated from the Okinawan bivalve *Pinna muricata*, are the most active members of the pinnatoxin family of marine toxins.[437] The $LD_{99}$ of the isolated 1:1 mixture of **693** and **694** was 22 μg/kg. By chemical transformations, the absolute stereochemistries of **693** and **694** were equated to the synthetically defined absolute stereochemistry of pinnatoxin A.[438] The structurally related pteriatoxins A-C **695**-**697** were isolated from the bivalve *Pteria penguin*.[439] Based upon spectroscopic similarities, the absolute stereochemistry of the polyether macrocyclic core of the toxins was proposed to be the same as that observed for the pinnatoxins. The absolute stereochemistry of pinnamine **698**, a toxin isolated from *Pinna muricata*,[440] has been confirmed by synthesis.[441] The absolute stereochemistry of pinnaic acid **699**, a toxin also isolated from *P. muricata*,[442] has

been secured by a combination of synthetic and degradative studies.[443] Two new members of the AZP (azaspiracid poisoning) inducing class of toxins **700** and **701** were reported from a collection of the mussel *Mytilus edulis*.[444] The absolute configuration at C-3 was secured by degradation of **701** and comparison with synthesised fragments. Five carotenoids **702**-**706** have been reported from the oyster *Crassostrea gigas*[445] and carotenoids **707**-**711** were also reported from the spindle shell *Fusinus perplexus*.[446] Two novel fatty acids **712** and **713** were isolated from the siphonarid limpet *Siphonaria denticulata*. The structures were confirmed by synthesis.[447]

## 10 Tunicates (ascidians)

The chemistry of ascidians continues to be dominated by amino acid-derived metabolites, although there are a growing number of examples based upon terpene and alkyl biosynthesis. A collection of the Mediterranean tunicate *Sidnyum turbinatum* afforded a range of antiproliferative alkyl sulfates **714**-**717**[448] while subsequent further examination of the same species afforded turbinamide **718**, a novel cytotoxic sulfated polyhydroxylated amide.[449] Continued investigation of the Brazilian ascidian *Didemnum granulatum* has led to the isolation of the novel alkaloid 6-bromogranulatimide **719**, and the known analogue granulatimide **720**, confirming the latter as a natural product.[450] Meridianins A **721** and C-E **722**-**724**, originally isolated from *Aplidium meridianum*,[451] have been synthesised in good yield from *N*-tosyl-acetylindoles.[452] Segoline C **725**, the enantiomer of previously reported segoline B,[453] has been reported from an Indian Ocean collection of *Eudistoma bituminis*.[454] Differences observed in the $^{13}C$ NMR data for segolines C and B suggests some discrepancies with the earlier assignments of segoline B resonances. The (–) enantiomer of 1,2,3-trithiane **726**, previously isolated as the (+) enantiomer from *Aplidium* sp.[455] has been reported from

the New Zealand ascidian *Hypsistozoa fasmeriana*.[456] The structurally related alkaloids fasmerianamine A **727** and B **728** were also reported from the ascidian. In two separate accounts, nine mono- and di-chlorinated diterpenoids, the haterumaimides A-I **729**-**737** were isolated as cytotoxic components from Okinawan collections of *Lissoclinum* sp.[457,458] The absolute stereochemistries of **729**-**732** and **735**-**737** were determined by chemical modification and application of the modified Mosher's method, while relative stereochemistries were determined for **733** and **734** only. A full account of the synthesis of tamandarin A **738** and B **739**, cytotoxic cyclic depsipeptides isolated from a Brazilian collection of an unidentified didemnid ascidian,[459] and related compounds, has been reported.[460] The methyl ester derivatives of previously reported endoperoxide stolonoxides A **740** and C **741**, isolated from *Stolonica socialis*[461,462] have been identified as potent inhibitors of the mitochondrial respiratory chain.[463] The absolute stereochemistry of minalemine A **742**, originally isolated from *Didemnum rodriguesi,*[464] has been defined by stereospecific synthesis.[465] The ascidian *Pseudodistoma obscurum* collected in Cadiz, Spain, has afforded the unsaturated amino alcohols **743**-**748** of which **744**-**748** were characterised as the diacetate derivatives.[466] The absolute configuration of **743** was determined as (2*S*,3*R*) by Mosher's method. The first syntheses of (–)-lepadins A **749** and C **750**, and a new synthesis of (–)-lepadin B **751** have been reported,[467] confirming the relative and establishing the absolute configuration of the alkaloids first reported from *Clavelina lepadiformis*.[468,469] A South African collection of *Pseudodistoma* sp. yielded four alkaloids, comprising three aliphatic amines **752-754** and a β-carboline alkaloid **755**.[470] Mosher's methodology was used to assign the absolute configuration of **752**. Two monocyclic piperidine alkaloids, uoamines A **756** and B **757** have been reported from the ascidian *Aplidium uouo*.[471] The structure of a modified pterin **758** isolated from a Fijian *Eudistoma* species of ascidian was secured using $^{1}H$-$^{15}N$ NMR spectroscopic techniques,[472] while the trimethylguanine derivative **759** was reported

from the New Zealand ascidian *Lissoclinum notti*.[473] Three members of the eudistomin-family of alkaloids **760**-**762** were reported from the ascidian *Eudistoma gilboverde* collected in Palau.[474] An Australian collection of *Polycarpa aurata* contained three simple *p*-methoxybenzoyl derivatives **763**-**765**.[475] The first example of a marine alkaloid bearing the rare *N*-*O*-methylindole functionality, pibocin B **766** was isolated from a *Eudistoma* sp. ascidian collected in the Sea of Japan.[476] A simple biomimetic synthesis of the pyridoacridine alkaloid styelsamine B **767**, isolated from an Indonesian collection of *Eusynstyela latericius*,[477] has been reported.[478] Mild oxidation of styelsamine B yielded cystodytin J **768**.[479] In two elegant accounts, total synthesis has dictated that the structures originally proposed for (–)-diazonamide A and B[480] be revised to **769**[481] and **770**[482] respectively. A ceramide derivative **771** was isolated from a Dayawan Bay collection of *Styela canopus*.[483] An antimicrobial 6.2 kDa peptide, dicynthaurin **772** which is comprised of two 30-residue monomers, has been reported from hemocytes of the solitary ascidian *Halocynthia aurantium*.[484] Investigation of the hemocytes of *S. clava* has afforded the clavanins and styelins, high molecular weight α-helical antimicrobial peptides.[485]

## 11 Echinoderms

The sea cucumber *Holothuria leucospilota* has afforded three ganglioside molecular species **773**-**775**. The structures of the ceramide portion of all three species are heterogeneous mixtures of alkyl homologues.[486] Studies of the star fish *Asterias rathbuni* collected in the Bering Sea resulted in the isolation of two novel steroidal glycosides **776** and **777**.[487] Two saponins, frondoside F **778** and $E_2$ **779** were isolated from a collection of the sea cucumber *Cucumaria frondosa*.[488] Two new steroids **780** and **781** have been reported from the Pacific starfish *Lysastrosoma anthosticta*.[489] Novel gangliosides CJP2 **782** and CJP3 **783** were

isolated from the feather star *Comanthus japonica*.[490] The starfish *Aphelasterias japonica* yielded four sulfated steroids, including the new example **784**.[491] Two sulfated triterpene glycosides with anti-HSV activity **785** and **786** were reported from the Antarctic sea cucumber *Staurocucumis liouvillei*.[492] Four novel nonmethylene-interrupted polyunsaturated fatty acid derivatives **787**-**790** were identified in extracts of the brittle star *Ophiura sarsi*.[493] Hedathiosulfonic acids A **791** and B **792** were isolated as acute toxicity-exhibiting constituents of the deep-sea urchin *Echinocardium cordatum*.[494] A triterpene glycoside patagonicoside A **793**, bearing a novel aglycon moiety, was reported from the sea cucumber *Psolus patagonicus*.[495] The glycoside exhibited potent antifungal activity towards the pathogen *Cladosporium cucumerinum*.

## 12 Conclusions

Over the previous 30 years there has been a marked increase in the number of marine natural products reported annually. During the period 1996-2000 there was, however, a decrease in the number of new compounds reported and the numbers for 2001 are following the same trend (Figure 1). These numbers suggest we are observing a lessening in the rate of discovery of new compounds from the marine environment. [496,497]

Also depicted graphically in Figure 1 is the rate of discovery of N-containing compounds over the same period. [496] The relative dearth of N-containing compounds reported earlier has been well compensated for in recent years, which is perhaps a reflection of the greater emphasis that is now placed on finding bioactive compounds. Of course, bioactivity could also be correlated with other possible structural indicators such as polyethers.

The breakdown of discoveries by phylum for 2001 is shown graphically in Figure 2. Sponges continue to dominate as a source of new compounds followed by coelenterates and the grouping of microorganisms and phytoplankton.

Insert Figures 1 & 2

## 13 Acknowledgements

We thank Eleanor Becker, Liesl Marsh, Kathryn Stillwell and Ekkehard Unger for assistance in collecting data for the preparation of this review.

## 14 References

1 D. J. Faulkner, *Nat. Prod. Rep.*, 1984, **1**, 251.

2 D. J. Faulkner, *Tetrahedron*, 1977, **33**, 1421.

3 A. B. Da Rocha, R. M. Lopes and G. Schwartsmann, *Curr. Opin. Pharmacol.*, 2001, **1**, 364.

4 R. X. Tan and W. X. Zou, *Nat. Prod. Rep.*, 2001, **18**, 448.

5 S. Hibino and T. Choshi, *Nat. Prod. Rep.*, 2001, **18**, 66.

6 J. R. Hanson, *Nat. Prod. Rep.*, 2001, **18**, 88.

7 B. R. O'Keefe, *J. Nat. Prod.*, 2001, **64**, 1373.

8 S. S. Yang, G. M. Cragg, D. J. Newman and J. P. Bader, *J. Nat. Prod.*, 2001, **64**, 265.

9 A. M. Burja, B. Banaigs, E. Abou-Mansour, J. Grant Burgess and P. C. Wright, *Tetrahedron*, 2001, **57**, 9347.

10 J. Patocka, *Acta Med.*, 2001, **44**, 69.

11 W. H. Gerwick, L. T. Tan and N. Sitachitta, *Alkaloids Chem. Biol.*, 2001, **57**, 75.

12 Y. Geng, X. Zhang and X. Zhao, *Tianran Chanwu Yanjiu Yu Kaifa*, 2001, **13**, 73.

13 T. K. Chakraborty and S. Das, *Curr. Med. Chem.: Anti Cancer Agents*, 2001, **1**, 131.

14 K. Miyazawa and T. Noguchi, *J. Toxicol. Toxin Rev.*, 2001, **20**, 11.

15 L. Mos, *Environ. Toxicol. Pharmacol.*, 2001, **9**, 79.

16 V. Burgess and G. Shaw, *Environment International,* 2001, **27**, 275.

17 Y. Wang, S. Yan, J. Su, L. Zeng and H. Li, *Youji Huaxue*, 2001, **21**, 16.

18 T. Matsuno, *Fish. Sci.*, 2001, **67**, 771.

19 U. Pindur and T. Lemster, *Curr. Med. Chem.*, 2001, **8**, 1681.

20 C. Jiménez, *Stud. Nat. Prod. Chem.*, 2001, **25**, 811.

21 C. D. Amsler, K. B. Iken, J. B. McClintock and B. J. Baker, *Mar. Chem. Ecol.*, (CRC Press LLC, Boca Raton, Fla) 2001, 267.

22 S. H. Sennett, *ibid*, 523.

23 G. Cimino and M. T. Ghiselin, *ibid*, 115.

24 G. Blunden, *Phytother. Res.*, 2001, **15**, 89.

25 R. J. Capon, *Eur. J. Org. Chem.*, 2001, **4**, 633.

26 A. M. S. Mayer and V. K. B. Lehmann, *Anticancer Res.*, 2001, **21**, 2489.

27 G. Schwartsmann, A. Brondani da Rocha, R. G. S. Berlinck and J. Jimeno, *Lancet Oncol.*, 2001, **2**, 221.

28 B. Austin, in "Recent Advances in Marine Biotechnology: Volume 6 Bio-organic Compounds: Chemistry and Biomedical Applications", ed. M. Fingerman and R. Nagabhushanam, Science Publishers, Inc., New Hampshire, USA, 2001, 1.

29 M. Kuniyoshi and T. Higa, *ibid*, 21.

30 F. M. Y. Faith, *ibid*, 85.

31 Y. Venkateswarlu, N. Srinivasa Reddy and U. Venkatesham, *ibid*, 101.

32 G. Anderluh and G. Menestrina, *ibid*, 131.

33 R. G. Kerr, A. C. Kohl and J. M. Boehnlein, *ibid*, 149.

34 M. R. Prinsep, *ibid*, 165.

35 W. R. Kem, *ibid*, 187.

36 C. de Albuquerque, A. Muhlia-Almazán, P. Hernández-Cortés and F. L. García-Carreño, *ibid*, 209.

37 D. Rittschof and K. K. Parker, *ibid*, 239.

38 J. Pei, J. Lei, T. Peng and J. Zhou, *Jisuanji Yu Yingyong Huaxue,* 2001, **18**, 353.

39 MarinLit database, Department of Chemistry, University of Canterbury, http://www.chem.canterbury.ac.nz/research/marinlit.htm

40 J. Muldoon, A. S. Shashkov, S. N. Senchenkova, S. V. Tomshich, N. A. Komandrova, L. A. Romanenko, Y. A. Knirel and A. V. Savage, *Carbohydr. Res.*, 2001, **330**, 231.

41 V. Ivanova, M. Oriol, M.-J. Montes, A. García and J. Guinea, *Z. Naturforsch. C Biosci.*, 2001, **56**, 1.

42 K. W. Cho, H.-S. Lee, J.-R. Rho, T. S. Kim, S. J. Mo and J. Shin, *J. Nat. Prod.*, 2001, **64**, 664.

43 I. Gonthier, M.-N. Rager, P. Metzger, J. Guezennec and C. Largeau, *Tetrahedron Lett.*, 2001, **42**, 2795.

44 R. de Nys, N. Kumar, K. A. Sharara, S. Srinivasan, G. Ball and S. Kjelleberg, *J. Nat. Prod.*, 2001, **64**, 531.

45 K. Gustafson, M. Roman and W. Fenical, *J. Am. Chem. Soc.*, 1989, **111**, 7519.

46 T. Nagao, K. Adachi, M. Sakai, M. Nishijima and H. Sano, *J. Antibiot.*, 2001, **54**, 333.

47 T. Barsby, M. T. Kelly, S. M. Gagné and R. J. Andersen, *Org. Lett.*, 2001, **3**, 437.

48 R. Fudou, T. Iizuka, S. Sato, T. Ando, N. Shimba and S. Yamanaka, *J. Antibiot.*, 2001, **54**, 153.

49 R. Fudou, T. Iizuka and S. Yamanaka, *J. Antibiot.*, 2001, **54**, 149.

50 E. Ohta, S. Ohta, N. K. Kubota, M. Suzuki, T. Ogawa, A. Yamasaki and S. Ikegami, *Tetrahedron Lett.*, 2001, **42**, 4179.

51 E. Ohta, N. K. Kubota, S. Ohta, M. Suzuki, T. Ogawa, A. Yamasaki and S. Ikegami, *Tetrahedron*, 2001, **57**, 8463.

52 H. He, W.-D. Ding, V. S. Bernan, A. D. Richardson, C. M. Ireland, M. Greenstein, G. A. Ellestad and G. T. Carter, *J. Am. Chem. Soc.*, 2001, **123**, 5362.

53 F. Romero, F. Espliego, J. Perez Baz, T. Garcia de Quesada, D. Gravalos, F. de la Calle and J. L. Fernandez-Puentes, *J. Antibiot.*, 1997, **50**, 734.

54 J. Perez Baz, L. M. Canedo, J. L. Fernandez Puentes and M. V. Silva Elipe, *J. Antibiot.*, 1997, **50**, 738.

55 D. L. Boger, S. Ichikawa, W. C. Tse, M. P. Hedrick and Q. Jin, *J. Am. Chem. Soc.*, 2001, **123**, 561.

56 R. W. Schumacher, B. L. Harrigan and B. S. Davidson, *Tetrahedron Lett.*, 2001, **42**, 5133.

57 A. A. Smelcerovic, S. M. Dordevic and R. M. Palic, *Hemijska Industrija*, 2001, **55**, 399.

58 S. Sperry, G. J. Samuels and P. Crews, *J. Org. Chem.*, 1998, **63**, 10011.

59 J. L. Wood, B. D. Thompson, N. Yusuff, D. A. Pflum and M. S. P. Matthäus, *J. Am. Chem. Soc.*, 2001, **123**, 2097.

60 H. Li, Y. Lin, L. Wang, S. Zhou and L. L. P. Vrijmoed, *Zhongshan Daxue Xuebao, Ziran Kexueban*, 2001, **40**, 70.

61 J. Wan, Y. Lin, X. Wu, S. Zhou and L. L. P. Vrijmoed, *Zhongshan Daxue Xuebao, Ziran Kexueban*, 2001, **40**, 127.

62 Y. Lin, X. Wu, S. Feng, G. Jiang, J. Luo, S. Zhou, L. L. P. Vrijmoed, E. B. G. Jones, K. Krohn, K. Steingröver and F. Zsila, *J. Org. Chem.*, 2001, **66**, 6252.

63 Y. Lin, X. Wu, S. Feng, G. Jiang, S. Zhou, L. L. P. Vrijmoed and E. B. Gareth Jones, *Tetrahedron Lett.*, 2001, **42**, 449.

64 R. Uchida, H. Tomoda, M. Arai and S. Omura, *J. Antibiot.*, 2001, **54**, 882.

65 W. H. Lin, H. Z. Fu, J. Li and P. Proksch, *Chin. Chem. Lett.*, 2001, **12**, 235.

66 W. H. Lin, J. Li, H. Z. Fu and P. Proksch, *Chin. Chem. Lett.*, 2001, **12**, 435.

67 H. Ui, K. Shiomi, Y. Yamaguchi, R. Masuma, T. Nagamitsu, D. Takano, T. Sunazuka, M. Namikoshi and S. Omura, *J. Antibiot.*, 2001, **54**, 234.

68 J.-R. Dai, B. K. Carte, P. J. Sidebottom, A. L. S. Yew, S.-B. Ng, Y. Huang and M. S. Butler, *J. Nat. Prod.*, 2001, **64**, 125.

69 M. Namikoshi, K. Akano, S. Meguro, I. Kasuga, Y. Mine, T. Takahashi and H. Kobayashi, *J. Nat. Prod.*, 2001, **64**, 396.

70 T. Yamada, M. Iritani, M. Doi, K. Minoura, T. Ito and A. Numata, *J. Chem. Soc. Perkin Trans. 1*, 2001, 3046.

71 L. A. McDonald, D. R. Abbanat, L. R. Barbieri, V. S. Bernan, C. M. Discafani, M. Greenstein, K. Janota, J. D. Korshalla, P. Lassota, M. Tischler and G. T. Carter, *Tetrahedron Lett.*, 1999, **40**, 2489.

72 T. Wang, O. Shirota, K. Nakanishi, N. Berova, L. A. McDonald, L. R. Barbieri and G. T. Carter, *Can. J. Chem.*, 2001, **79**, 1786.

73 M. Cueto, P. R. Jensen, C. Kauffman, W. Fenical, E. Lobkovsky and J. Clardy, *J. Nat. Prod.*, 2001, **64**, 1444.

74 M. Chinworrungsee, P. Kittakoop, M. Isaka, A. Rungrod, M. Tanticharoen and Y. Thebtaranonth, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 1965.

75 A. Miljkovic, P. G. Mantle, D. J. Williams and B. Rassing, *J. Nat. Prod.*, 2001, **64**, 1251.

76 K. Komatsu, H. Shigemori and J. Kobayashi, *J. Org. Chem.*, 2001, **66**, 6189.

77 G. Brauers, R. Ebel, R. Edrada, V. Wray, A. Berg, U. Gräfe and P. Proksch, *J. Nat. Prod.*, 2001, **64**, 651.

78 R. Jadulco, P. Proksch, V. Wray, Sudarsono, A. Berg and U. Gräfe, *J. Nat. Prod.*, 2001, **64**, 527.

79 C. Iwamoto, T. Yamada, Y. Ito, K. Minoura and A. Numata, *Tetrahedron*, 2001, **57**, 2997.

80 H. Luesch, W. Y. Yoshida, R. E. Moore, V. J. Paul and T. H. Corbett, *J. Am. Chem. Soc.*, 2001, **123**, 5418.

81 H. Luesch, R. Pangilinan, W. Y. Yoshida, R. E. Moore and V. J. Paul, *J. Nat. Prod.*, 2001, **64**, 304.

82 J. Orjala, D. G. Nagle, V. Hsu and W. H. Gerwick, *J. Am. Chem. Soc.*, 1995, **117**, 8281.

83 L. M. Nogle, T. Okino and W. H. Gerwick, *J. Nat. Prod.*, 2001, **64**, 983.

84 R. Kazlauskas, R. O. Lidgard and R. J. Wells, *Tetrahedron Lett.*, 1977, **18**, 3183.

85 C. Charles, J. C. Braekman, D. Daloze, B. Tursch and R. Karlsson, *Tetrahedron Lett.*, 1978, 1519.

86 J. I. Jiménez and P. J. Scheuer, *J. Nat. Prod.*, 2001, **64**, 200.

87 G. G. Harrigan, H. Luesch, W. Y. Yoshida, R. E. Moore, D. G. Nagle and V. J. Paul, *J. Nat. Prod.*, 1999, **62**, 655.

88 G. R. Pettit, Y. Kamano, C. L. Herald, C. Dufresne, R. L. Cerny, D. L. Herald, J. M. Schmidt and H. Kizu, *J. Am. Chem. Soc.*, 1989, **111**, 5015.

89 L. M. Nogle, R. T. Williamson and W. H. Gerwick, *J. Nat. Prod.*, 2001, **64**, 716.

90 H. Luesch, W. Y. Yoshida, R. E. Moore, V. J. Paul and S. L. Mooberry, *J. Nat. Prod.*, 2000, **63**, 611.

91 F. Yokokawa, H. Sameshima and T. Shioiri, *Tetrahedron Lett.*, 2001, **42**, 4171.

92 B. W. Son, J. C. Kim and H. D. Choi, *Lipids*, 2001, **36**, 427.

93 G. G. Harrigan, H. Luesch, W. Y. Yoshida, R. E. Moore, D. G. Nagle, V. J. Paul, S. L. Mooberry, T. H. Corbett and F. A. Valeriote, *J. Nat. Prod.*, 1998, **61**, 1075.

94 H. Luesch, R. E. Moore, V. J. Paul, S. L. Mooberry and T. H. Corbett, *J. Nat. Prod.*, 2001, **64**, 907.

95 G. R. Pettit, Y. Kamano, C. L. Herald, Y. Fujii, H. Kizu, M. R. Boyd, F. E. Boettner, D. L. Doubek, J. M. Schmidt, J.-C. Chapuis and C. Michel, *Tetrahedron*, 1993, **49**, 9151.

96 M. A. Orsini, L. K. Pannell and K. L. Erickson, *J. Nat. Prod.*, 2001, **64**, 572.

97 T. Igarashi, M. Satake and T. Yasumoto, *J. Am. Chem. Soc.*, 1996, **118**, 479.

98 M. Sasaki, T. Shida and K. Tachibana, *Tetrahedron Lett.*, 2001, **42**, 5725.

99 F. Dini, G. Guella, P. Giubbilini, I. Mancini and F. Pietra, *Naturwissenschaften*, 1993, **80**, 84.

100 R. A. Aungst and R. L. Funk, *J. Am. Chem. Soc.*, 2001, **123**, 9455.

101 T. Ukena, M. Satake, M. Usami, Y. Oshima, H. Naoki, T. Fujita, Y. Kan and T. Yasumoto, *Biosci. Biotechnol. Biochem.*, 2001, **65**, 2585.

102 Y. Kan, D. Uemura, Y. Hirata, M. Ishiguro and T. Iwashita, *Tetrahedron Lett.*, 2001, **42**, 3197.

103 M. Tsuda, T. Endo, J. Kobayashi, *J. Org. Chem.*, 2000, **65**, 1349.

104 J. Kobayashi, T. Kubota, T. Endo and M. Tsuda, *J. Org. Chem.*, 2001, **66**, 134.

105 T. Kubota, T. Endo, M. Tsuda, M. Shiro and J. Kobayashi, *Tetrahedron*, 2001, **57**, 6175.

106 J. Kobayashi, M. Ishibashi, M. R. Wälchli, H. Nakamura, Y. Hirata, T. Sasaki and Y. Ohizumi, *J. Am. Chem. Soc.*, 1988, **110**, 490.

107 T. Kubota, M. Tsuda and J. Kobayashi, *Org. Lett.*, 2001, **3**, 1363.

108 M. Ishibashi, M. Sato and J. Kobayashi, *J. Org, Chem.*, 1993, **58**, 6928.

109 D. R. Williams and K. G. Meyer, *J. Am. Chem. Soc.*, 2001, **123**, 765.

110 T. Hu, J. M. Curtis, J. A. Walter, Y. Oshima, M. A. Quilliam and J. L. C. Wright, *J. Chem. Soc. Chem. Commun.*, 1995, 2159.

111 T. Hu, I. W. Burton, A. D. Cembella, J. M. Curtis, M. A. Quilliam, J. A. Walter and J. L. C. Wright, *J. Nat. Prod.*, 2001, **64**, 308.

112 D. Uemura, T. Chou, T. Haino, A. Nagatsu, S. Fukuzawa, S. Zheng and H. Chen, *J. Am. Chem. Soc.*, 1995, **117**, 1155.

113 T. Chou, O. Kamo and D. Uemura, *Tetrahedron Lett.*, 1996, **37**, 4023.

114 T. Chou, T. Haino, M. Kuramoto and D. Uemura, *Tetrahedron Lett.*, 1996, **37**, 4027.

115 M. Falk, I. W. Burton, T. Hu, J. A. Walter and J. L. C. Wright, *Tetrahedron*, 2001, **57**, 8659.

116 C.-K. Lu, G.-H. Lee, R. Huang and H.-N. Chou, *Tetrahedron Lett.*, 2001, **42**, 1713.

117 B. Suárez-Gómez, M. L. Souto, M. Norte and J. J. Fernández, *J. Nat. Prod.*, 2001, **64**, 1363.

118 S. T. Belt, W. G. Allard, G. Massé, J.-M. Robert and S. J. Rowland, *Tetrahedron Lett.*, 2001, **42**, 5583.

119 B. W. Son, Y. J. Cho, J. S. Choi, W. K. Lee, D.-S. Kim, H. D. Choi, J. H. Jung, K. S. Im and W. C. Choi, *Nat. Prod. Lett.*, 2001, **15**, 299.

120 M. T. Hamann and P. J. Scheuer, *J. Am. Chem. Soc.*, 1993, **115**, 5825.

121 A. López-Macià, J. C. Jiménez, M. Royo, E. Giralt and F. Albericio, *J. Am. Chem. Soc.*, 2001, **123**, 11398.

122 G. Goetz, W. Y. Yoshida and P. J. Scheuer, *Tetrahedron*, 1999, **55**, 7739.

123 M. S. Ali, M. Saleem, V. U. Ahmad and S. Shameel, *Z. Naturforsch. B Chem. Sci.*, 2001, **56**, 837.

124 S.-E. N. Ayyad, M. O. Slama, A. H. MoKhtar and A. F. Anter, *Boll. Chim. Farm.*, 2001, **140**, 155.

125 N. Takada, R. Watanabe, K. Suenaga, K. Yamada and D. Uemura, *J. Nat. Prod.*, 2001, **64**, 653.

126 X. H. Xu, X. Chen, J. H. Lu, G. M. Yao and Y. M. Li, *Chin. Chem. Lett.*, 2001, **12**, 709.

127 M. Cortés, J. A. Valderrama, M. Cuellar, V. Armstrong and M. Preite, *J. Nat. Prod.*, 2001, **64**, 348.

128 G. Culioli, M. Daoudi, A. Ortalo-Magné, R. Valls and L. Piovetti, *Phytochemistry*, 2001, **57**, 529.

129 Atta-ur-Rahman, M. I. Choudhary, S. Hayat, A. M. Khan and A. Ahmed, *Chem. Pharm. Bull.*, 2001, **49**, 105.

130 A. K. Holmeide, l. Skattebol and M. Sydnes, *J. Chem. Soc. Perkin Trans. 1*, 2001, 1942.

131 T. G. Halsall and I. R. Hills, *J. Chem. Soc. Chem. Commun.*, 1971, 448.

132 X. Xu, J. Lu, G. Yao, Y. Li, J. Su and L. Zeng, *Tianran Chanwu Yanjiu Yu Kaifa*, 2001, **13**, 5.

133 G. Guella, I. Mancini, G. Chiasera and F. Pietra, *Helv. Chim. Acta*, 1992, **75**, 310.

134 R. Matsumura, T. Suzuki, H. Hagiwara, T. Hoshi and M. Ando, *Tetrahedron Lett.*, 2001, **42**, 1543.

135 K. Ohta and M. Takagi, *Phytochemistry*, 1977, **16**, 1062-3.

136 D. C. Harrowven, M. C. Lucas and P. D. Howes, *Tetrahedron*, 2001, **57**, 791.

137 M. T. Crimmins and K. A. Emmitte, *J. Am. Chem. Soc.*, 2001, **123**, 1533.

138 M. Suzuki, M. Daitoh, C. S. Vairappan, T. Abe and M. Masuda, *J. Nat. Prod.*, 2001, **64**, 597.

139 A. Rudi and Y. Kashman, *J. Nat. Prod.*, 1992, **55**, 1408.

140 M. Kuniyoshi, M. S. Marma, T. Higa, G. Bernardinelli and C. W. Jefford, *J. Nat. Prod.*, 2001, **64**, 696.

141 M. E. Y. Francisco and K. L. Erickson, *J. Nat. Prod.*, 2001, **64**, 790.

142 D. Davyt, R. Fernandez, L. Suescun, A. W. Mombrú, J. Saldaña, L. Domínguez, J. Coll, M. T. Fujii and E. Manta, *J. Nat. Prod.*, 2001, **64**, 1552.

143 L. Suescun, A. W. Mombrú, R. A. Mariezcurrena, D. Davyt, R. Fernández and E. Manta, *Acta Crystallogr. Sect. C.*, 2001, **57**, 286.

144 E. G. Juagdan, R. Kalidindi and P. J. Scheuer, *Tetrahedron*, 1997, **53**, 521.

145 C. P. Manríquez, M. L. Souto, J. A. Gavín, M. Norte and J. J. Fernández, *Tetrahedron*, 2001, **57**, 3117.

146 G. Guella, D. Skropeta, S. Breuils, I. Mancini and F. Pietra, *Tetrahedron Lett.*, 2001, **42**, 723.

147 C. S. Vairappan, M. Daitoh, M. Suzuki, T. Abe and M. Masuda, *Phytochemistry*, 2001, **58**, 291.

148 C. S. Vairappan, M. Suzuki, T. Abe and M. Masuda, *Phytochemistry*, 2001, **58**, 517.

149 N. Mihopoulos, C. Vagias, E. Mikros, M. Scoullos and V. Roussis, *Tetrahedron Lett.*, 2001, **42**, 3749.

150 X.-H. Xu, X. Chen, J.-H. Lu, G.-M. Yao, Y.-M. Li and L.-M. Zheng, *Chin. J. Chem.*, 2001, **19**, 702.

151 J.-M. Lo, W.-L. Wang, Y.-M. Chiang and C.-M. Chen, *J. Chin. Chem. Soc.*, 2001, **48**, 821.

152 M. L. Ciavatta, S. Wahidulla, L. D'Souza, G. Scognamiglio and G. Cimino, *Tetrahedron*, 2001, **57**, 617.

153 J. Darias, J. Rovirosa, A. San-Martin, A.-R. Díaz, E. Dorta and M. Cueto, *J. Nat. Prod.*, 2001, **64**, 1383.

154 T. Rezanka and V. M. Dembitsky, *Phytochemistry*, 2001, **57**, 607.

155 S. Etahiri, V. Bultel-Poncé, C. Caux and M. Guyot, *J. Nat. Prod.*, 2001, **64**, 1024.

156 P. Ramesh, V. Ravikanth, V. L. N. Reddy, T. V. Goud and Y. Venkateswarlu, *J. Chem. Res. Synop.*, 2001, 232.

157 Y. Nakao, K. Takada, S. Matsunaga and N. Fusetani, *Tetrahedron*, 2001, **57**, 3013.

158 B. N. Zhou, M. P. Mattern, R. K. Johnson and D. G. I. Kingston, *Tetrahedron*, 2001, **57**, 9549.

159 N. Borbone, S. De Marino, M Iorizzi, F. Zollo, C. Debitus, A. Ianaro and B. Pisano, *Eur. J. Org. Chem.*, 2001, 4651.

160 R. J. Clark, M. J. Garson and J. N. A. Hooper, *J. Nat. Prod.*, 2001, **64**, 1568.

161 M. Seki, A. Kayo and K. Mori, *Tetrahedron Lett.*, 2001, **42**, 2357.

162 M. Seki and K. Mori, *Eur. J. Org. Chem.*, 2001, 3797.

163 V. Costantino, E. Fattorusso, A. Mangoni, M. Di Rosa and A. Ianaro, *J. Am. Chem. Soc.*, 1997, **119**, 12465.

164 Y. C. Shen, C. V. S. Prakash and Y. H. Kuo, *J. Nat. Prod.*, 2001, **64**, 324.

165 N. Alam, B. H. Bae, J. Hong, C. O. Lee, B. A. Shin, K. S. Im and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 533.

166 N. M. Carballeira and M. Pagan, *J. Nat. Prod.*, 2001, **64**, 620.

167 S. Matsunaga, S. Nishimura and N. Fusetani, *J. Nat. Prod.*, 2001, **64**, 816.

168 H. Niwa, K. Wakamatsu and K. Yamada, *Tetrahedron Lett.*, 1989, **30**, 4543.

169 Y. Baba, G. Saha, S. Nakao, C. Iwata, T. Tanaka, T. Ibuka, H. Ohishi and Y. Takemoto, *J. Org. Chem.*, 2001, **66**, 81.

170 R. J. Capon, C. Skene, E. H. Liu, E. Lacey, J. H. Gill, K. Heiland and T. Friedel, *J. Org. Chem.*, 2001, **66**, 7765.

171 A. Fontana, G. d'Ippolito, L. D'Souza, E. Mollo, P. S. Parameswaram and G. Cimino, *J. Nat. Prod.*, 2001, **64**, 131.

172 Y. J. Lim, H. S. Park, K. S. Im, C. Lee, J. Hong, M. Lee, D. Kim and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 46.

173 Y. J. Lim, C. Lee, J. Hong, D. Kim, K. S. Im and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 1565.

174 M. Kobayashi, T. Mahmud, H. Tajima, W. Wang, S. Aoki, S. Nakagawa, T.Mayumi and I. Kitagawa, *Chem. Pharm. Bull.*, 1996, **44**, 720

175 B. W. Gung, H. Dickson and S. Shockley, *Tetrahedron Lett.*, 2001, **42**, 4761.

176 A. Zampella, C. Giannini, C. Debitus and M. V. D'Auria, *Tetrahedron*, 2001, **57**, 257.

177 E. Ohta, S. Ohta and S. Ikegami, *Tetrahedron*, 2001, **57**, 4699.

178 M. Fujita, Y. Nakao, S. Matsunaga, M. Seiki, Y. Itoh, R. W. M. van Soest and N. Fusetani, *Tetrahedron*, 2001, **57**, 1229.

179 Y. Chen, K. B. Killday, P. J. McCarthy, R. Schimoler, K. Chilson, C. Selitrennikoff, S. A. Pomponi and A. E. Wright, *J. Nat. Prod.*, 2001, **64**, 262.

180 T. L. Perry, A. Dickerson, A. A. Khan, R. K. Kondru, D. N. Beratan, P. Wipf, M. Kelly and M. T. Hamann, *Tetrahedron*, 2001, **57**, 1483.

181 D. E. Williams, T. M. Allen, R. B. van Soest, W. Behrish and R. J. Andersen, *J. Nat. Prod.*, 2001, **64**, 281.

182 D. J. Faulkner, R. W. Armstrong, P. Djura, M. D. Higgs, B. N. Ravi, D. B. Stierle and S. J. Wratten, *Colloques internationaux du C.N.R.S.*, 1979, **291**, 401.

183 N. Takada, M. Watanabe, A. Yamada, K. Suenaga, K. Yamada, K. Ueda and D. Uemura, *J. Nat. Prod.*, 2001, **64**, 356.

184 J. F. Hu, H. F. Gao, M. Kelly and M. T. Hamann, *Tetrahedron*, 2001, **57**, 9379.

185 D. J. Gochfeld and M. T. Hamann, *J. Nat. Prod.*, 2001, **64**, 1477.

186 K. L. Erickson, J. A. Beutler, J. H. Cardellina II and M. R. Boyd, *J. Org. Chem.*, 1997, **62**, 8188.

187 K. L. Erickson, J. A. Beutler, J. H. Cardellina II and M. R. Boyd, *J. Org. Chem.*, 2001, **66**, 1532.

188 D. Labrecque, S. Charron, R. Rej, C. Blais and S. Lamothe, *Tetrahedron Lett.*, 2001, **42**, 2645.

189 B. B. Snider and F. Song, *Org. Lett.*, 2001, **3**, 1817.

190 A. Fürstner, D. Thorsten, O. R. Thiel and G. Blanda, *Chem. Eur. J.*, 2001, **7**, 5286.

191 R. Watanadilok, P. Sonchaeng, A. Kijjoa, A. M. Damas, L. Gales, A. M. S. Silva and W. Herz, *J. Nat. Prod.*, 2001, **64**, 1056.

192 D. Vuong, R. J. Capon, E. Lacey, J. H. Gill, K. Heiland and T. Friedel, *J. Nat. Prod.*, 2001, **64**, 640.

193 Z. Thale, F. R. Kinder, K. W. Bair, J. Bontempo, A. M. Czuchta, R. W. Versace, P. E. Phillips, M. L. Sanders, S. Wattanasin and P. Crews, *J. Org. Chem.*, 2001, **66**, 1733.

194 A. Grassia, I. Bruno, C. Debitus, S. Marzocco, A. Pinto, L. Gomez-Paloma and R. Riccio, *Tetrahedron*, 2001, **57**, 6257.

195 A. Cutignano, I. Bruno, G. Bifulco, A. Casapullo, C. Debitus, L. Gomez-Paloma and R. Riccio, *Eur. J. Org. Chem.*, 2001, **4**, 775.

196 A. B. Smith III, I. G. Safonov and R. M. Corbett, *J. Am. Chem. Soc.*, 2001, **123**, 12426.

197 J. Tanaka and T. Higa, *Tetrahedron Lett.*, 1996, **37**, 5535.

198 M. A. Rashid, K. R. Gustafson and M. R. Boyd, *Tetrahedron Lett.*, 2001, **42**, 1623.

199 M. A. Rashid, C. L. Cantrell, K. R. Gustafson and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 1341.

200 A. Randazzo, C. Debitus and L. Gomez-Paloma, *Tetrahedron*, 2001, **57**, 4443.

201 J. Tabudravu, L. A. Morris, J. J. Kettenes-van den Bosch and M. Jaspars, *Tetrahedron Lett.*, 2001, **42**, 9273.

202 L. T. Tan, R. T. Williamson and W. H. Gerwick, *J. Org. Chem.*, 2000, **65**, 419.

203 F. Yokokawa, H. Sameshima and T. Shioiri, *Synlett*, 2001, 986.

204 M. Tsuda, H. Shigemori, Y. Mikami and J. Kobayashi, *Tetrahedron*, 1993, **49**, 6785.

205 A. Napolitano, I. Bruno, P. Rovero, R. Lucas, M. P. Peris, L. Gomez-Paloma and R. Riccio, *Tetrahedron*, 2001, **57**, 6249.

206 G. R. Pettit, R. Tan, Y. Ichihara, M. D. Williams, D. L. Doubek, L. P. Tackett and J. M. Schmidt, *J. Nat. Prod.*, 1995, **58**, 961.

207 G. R. Pettit, J. W. Lippert III, S. R. Taylor, R. Tan and M. D. Williams, *J. Nat. Prod.*, 2001, **64**, 883.

208 M. A. Rashid, K. R. Gustafson, L. K. Cartner, N. Shigematsu, L. K. Pannell and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 117.

209 A. Randazzo, G. Bifulco, C. Giannini, M. Bucci, C. Debitus, G. Cirino and L. Gomez-Paloma, *J. Am. Chem. Soc.*, 2001, **123**, 10870.

210 L. L. Guan, Y. Sera, K. Adachi, F. Nishida and Y. Shizuri, *Biochem. Biophys. Res. Commun.*, 2001, **283**, 976.

211 R. Sakai, T. Koike, M. Sasaki, K. Shimamoto, C. Oiwa, A. Yano, K. Suzuki, K. Tachibana and H. Kamiya, *Org. Lett.*, 2001, **3**, 1479.

212 R. Sakai, C. Oiwa, K. Takaishi, H. Kamiya and M. Tagawa, *Tetrahedron Lett.*, 1999, **40**, 6941.

213 B. B. Snider and Y. Gu, *Org. Lett.*, 2001, **3**, 1761.

214 N. Dumrongchai, C. Ponglimanont, B. L. Stapleton and M. J. Garson, *ACGC Chem. Res. Commun.*, 2001, **13**, 17.

215 B. L. Stapleton, G. M. Cameron and M. J. Garson, *Tetrahedron*, 2001, **57**, 4603.

216 G. G. Harrigan, G. H. Goetz, H. Luesch, S. Yang and J. Likos, *J. Nat. Prod.*, 2001, **64**, 1133.

217 S. Tsukamoto, K. Tane, T. Ohta, S. Matsunaga, N. Fusetani and R. W. M. van Soest, *J. Nat. Prod.*, 2001, **64**, 1576.

218 G. Koren-Goldshlager, Y. Kashman and M. Schleyer, *J. Nat. Prod.*, 1998, **61**, 282.

219 M. R. Heinrich and W. Steglich, *Tetrahedron Lett.*, 2001, **42**, 3287.

220 M. G. Banwell, A. M. Bray, A. J. Edwards and D. J. Wong, *New J. Chem.*, 2001, **25**, 1347.

221 M. R. Heinrich, Y. Kashman, P. Spiteller and W. Steglich, *Tetrahedron*, 2001, **57**, 9973.

222 S. Tsukamoto, H. Kato, H. Hirota and N. Fusetani, *Tetrahedron Lett.*, 1996, **37**, 5555.

223 D. Nozawa, H. Takikawa and K. Mori, *Bioorg. Med. Chem. Lett.*, 2001, **11**, 1481.

224 H. Takikawa, D. Nozawa and K. Mori, *J. Chem. Soc. Perkin Trans. 1*, 2001, 657.

225 J. Shin, Y. Seo, K. W. Cho, J. Rho and C. J. Sim, *J. Nat. Prod.*, 1997, **60**, 611.

226 N. Yamazaki, W. Dokoshi and C. Kibayashi, *Org. Lett.*, 2001, **3**, 193.

227 A. D. Patil, A. J. Freyer, P. B. Taylor, B. Carté, G. Zuber, R. K. Johnson and D. J. Faulkner, *J. Org. Chem.*, 1997, **62**, 1814.

228 J. C. Braekman, D. Daloze, R. Tavares, E. Hajdu and R. W. M. van Soest, *J. Nat. Prod.*, 2000, **63**, 193.

229 F. Cohen and L. E. Overman, *J. Am. Chem. Soc.*, 2001, **123**, 10782.

230 R. J. Capon, M. Miller and F. Rooney, *J. Nat. Prod.*, 2001, **64**, 643.

231 T. Hattori, S. Matsuo, K. Adachi and Y. Shizuri, *Fish. Sci.*, 2001, **67**, 690.

232 J. Shin, J. R. Rho, Y. Seo, H. S. Lee, K. W. Cho, H. J. Kwon and C. J. Sim, *Tetrahedron Lett.*, 2001, **42**, 1965.

233 S. Carmely, M. Ilan and Y. Kashman, *Tetrahedron*, 1989, **45**, 2193.

234 I. Kawasaki, S. Nakamura, S. Yanagitani, A. Kakumo, M. Yamashita and S. Ohta, *J. Chem. Soc. Perkin Trans. 1*, 2001, 3095.

235 S. Aoki, Y. Ye, K. Higuchi, A. Takashima, Y. Tanaka, I. Kitagawa and M. Kobayashi, *Chem. Pharm. Bull.*, 2001, **49**, 1372.

236 S. C. Bobzin and D. J. Faulkner, *J. Org. Chem.*, 1991, **56**, 4403.

237 N. J. Lawrence and S. M. Bushell, *Tetrahedron Lett.*, 2001, **42**, 7671.

238 S. P. Gunasekera, P. J. McCarthy and M. Kelly-Borges, *J. Nat. Prod.*, 1994, **57**, 1437.

239 B. Jiang, C. G. Yang and J. Wang, *J. Org. Chem.*, 2001, **66**, 4865.

240 M. Kobayashi, Y. J. Chen, S. Aoki, Y. In, T. Ishida and I. Kitagawa, *Tetrahedron*, 1995, **51**, 3727.

241 B. E. A. Burm, P. Blokker, E. Jongmans, E. van Kampen, M. J. Wanner and G. J. Koomen, *Heterocycles*, 2001, **55**, 495.

242 K. A. El Sayed, M. Kelly, U. A. K. Kara, K. K. H. Ang, I. Katsuyama, D. C. Dunbar, A. A. Khan and M. T. Hamman, *J. Am. Chem. Soc.*, 2001, **123**, 1804.

243 M. Tsuda, K. Hirano, T. Kubota and J. Kobayashi, *Tetrahedron Lett.*, 1999, **40**, 4819.

244 B. B. Snider and B. Shi, *Tetrahedron Lett.*, 2001, **42**, 1639.

245 K. Hirano, T. Kubota, M. Tsuda, Y. Mikami and J. Kobayashi, *Chem. Pharm. Bull.*, 2000, **48**, 974.

246 N. B. Perry, L. Ettouati, M. Litaudon, J. W. Blunt and M. H. G. Munro, *Tetrahedron*, 1994, **50**, 3987.

247 R. J. Anderson and J. C. Morris, *Tetrahedron Lett.*, 2001, **42**, 8697.

248 M. A. Rashid, K. R. Gustafson and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 1249.

249 P. S. Parameswaran, C. G. Naik, S. Y. Kamat and B. N. Pramanik, *Indian J. Chem.*, 1998, **37B**, 1258.

250 N. Saito, H. Sakai, K. Suwanborirux, S. Pummangura and A. Kubo, *Heterocycles*, 2001, **55**, 21.

251 G. R. Pettit, J. C. Knight, J. C. Collins, D. L. Herald, R. K. Pettit, M. R. Boyd and V. G. Young, *J. Nat. Prod.*, 2000, **63**, 793.

252 A. Casapullo, A. Cutignano, I. Bruno, G. Bifulco, C. Debitus, L. Gomez-Paloma and R. Riccio, *J. Nat. Prod.*, 2001, **64**, 1354.

253 D. Tasdemir, K. M. Marshall, G. C. Mangalindan, G. P. Concepcion, L. R. Barrows, M. K. Harper and C. M. Ireland, *J. Org. Chem.*, 2001, **66**, 3246.

254 K. C. Bascombe, S. R. Peter, W. F. Tinto, S. M. Bissada, S. McLean and W. F. Reynolds, *Heterocycles*, 1998, **48**, 1461.

255 M. Seki and K. Mori, *Eur. J. Org. Chem.*, 2001, **3**, 503.

256 M. Tsuda, H. Uemoto and J. Kobayashi, *Tetrahedron Lett.*, 1999, **40**, 5709.

257 B. Jiang, J. F. Liu and S. Y. Zhao, *Org. Lett.*, 2001, **3**, 4011.

258 A. Rudi, Z. Stein, S. Green, I. Goldberg and Y. Kashman, *Tetrahedron Lett.*, 1994, **35**, 2589.

259 A. Radspieler and J. Liebscher, *Tetrahedron*, 2001, **57**, 4867.

260 M. Assmann, S. Zea and M. Kock, *J. Nat. Prod.*, 2001, **64**, 1593.

261 G. H. Goetz, G. G. Harrigan and J. Likos, *J. Nat. Prod.*, 2001, **64**, 1581.

262 M. Assmann, R. W. M. van Soest and M. Kock, *J. Nat. Prod.*, 2001, **64**, 1345.

263 M. Bourguet-Kondracki, M. Martin, J. Vacelet and M. Guyot, *Tetrahedron Lett.*, 2001, **42**, 7257.

264 D. Tasdemir, G. C. Mangalidan, G. P. Concepcion, M. K. Harper and C. M. Ireland, *Chem. Pharm. Bull.*, 2001, **49**, 1628.

265 K. B. Killday, D. Yarwood, M. A. Sills, P. T. Murphy, J. N. A. Hooper and A. E. Wright, *J. Nat. Prod.*, 2001, **64**, 525.

266 J. Kobayashi, K. Honma, T. Sasaki and M. Tsuda, *Chem. Pharm. Bull.*, 1995, **43**, 403.

267 T. R. Boehlow, J. J. Harburn and C. D. Spilling, *J. Org. Chem.*, 2001, **66**, 3111.

268 G. M. Nicholas, G. L. Newton, R. C. Fahey and C. A. Bewley, *Org. Lett.*, 2001, **3**, 1543.

269 N. Takada, R. Watanabe, K. Suenaga, K. Yamada, K. Ueda, M. Kita and D. Uemura, *Tetrahedron Lett.*, 2001, **42**, 5265.

270 T. Evan, A. Rudi, M. Ilan and Y. Kashman, *J. Nat. Prod.*, 2001, **64**, 226.

271 M. Tsuda, Y. Sakuma and J. Kobayashi, *J. Nat. Prod.*, 2001, **64**, 980.

272 P. Ciminiello, C. Dell'Aversano, E. Fattorusso and S. Magno, *Eur. J. Org. Chem.*, 2001, **1**, 55.

273 N. Fusetani, Y. Masuda, Y. Nakao, S. Matsunaga and R. W. M. van Soest, *Tetrahedron*, 2001, **57**, 7507.

274 A. Kijjoa, R. Watanadilok, P. Sonchaeng, A. M. S. Silva, G. Eaton and W. Herz, *Z. Naturforsch.* 2001, **56c**, 1116.

275 T. Hattori, A. Konno, K. Adachi and Y. Shizuri, *Fish. Sci.*, 2001, **67**, 899.

276 N. K. Utkina, V. A. Denisenko, O. V. Scholokova, M. V. Virovaya, A. V. Gerasimenko, D. Y. Popov, V. B. Krasokhin and A. M. Popov, *J. Nat. Prod.*, 2001, **64**, 151.

277 Y. Okamoto, M. Ojika, S. Suzuki, M. Murakami and Y. Sakagami, *Bioorg. Med. Chem.*, 2001, **9**, 179.

278 Y. Shen, C. Chen and Y. Kuo, *J. Nat. Prod.*, 2001, **64**, 801.

279 C. Giannini, C. Debitus, R. Lucas, A. Ubeda, M. Paya, J. N. A. Hooper and M. V. D'Auria, *J. Nat. Prod.*, 2001, **64**, 612.

280 H. Mitome, T. Nagasawa, H. Miyaoka, Y. Yamada and R. W. M. van Soest, *J. Nat. Prod.*, 2001, **64**, 1506.

281 M. L. Kondracki, D. Davoust and M. Guyot, *J. Chem. Res. Synop.*, 1989, **3**, 74.

282 H. Nakamura, S. Deng, J. Kobayashi, Y. Ohizumi and Y. Hirata, *Tetrahedron*, 1986, **42**, 4197.

283 Y. Haruo, T. Hasegawa, H. Tanaka and T. Takahashi, *Synlett,* 2001, 1935.

284 A. D. Patil, A. J. Freyer, L. Killmer, P. Offen, B. Carte, A. J. Jurewicz and R. K. Johnson, *Tetrahedron*, 1997, **53**, 5047.

285 M. Inoue, M. W. Carson, A. J. Frontier and S. J. Danishefsky, *J. Am. Chem. Soc.*, 2001, **123**, 1878.

286 J. Carroll, E. N. Jonsson, R. Ebel, M. S. Hartman, T. R. Holman and P. Crews, *J. Org. Chem.*, 2001, **66**, 6847.

287 M. Musman, I. I. Ohtani, D. Nagaoka, J. Tanaka and T. Higa, *J. Nat. Prod.*, 2001, **64**, 350.

288 A. Loukaci, I. Le Saout, M. Samadi, S. Leclerc, E. Damiens, L. Meijer, C. Debitus and M. Guyot, *Bioorg. Med. Chem.*, 2001, **9**, 3049.

289 S. Poigny, S. Nouri, A. Chiaroni, M. Guyot and M. Samadi, *J. Org. Chem.*, 2001, **66**, 7263.

290 M. R. Kernan and D. J. Faulkner, *J. Org. Chem.*, 1988, **53**, 4574.

291 G. H. Goetz, G. G. Harrigan and J. Likos, *J. Nat. Prod.*, 2001, **64**, 1486.

292 M. Musman, J. Tanaka and T. Higa, *J. Nat. Prod.*, 2001, **64**, 111.

293 S. Kehraus, G. M. König and A. D. Wright, *J. Nat. Prod.*, 2001, **64**, 939.

294 G. M. König and A. D. Wright, *J. Org. Chem.*, 1997, **62**, 3837.

295 G. Mehta and K. Srinivas, *Tetrahedron Lett.*, 2001, **42**, 2855.

296 S. Fietz-Razavian, S. Schulz, I. Dix and P. G. Jones, *Chem. Commun.*, 2001, 2154.

297 D. T. A. Youssef, W. Y. Yoshida, M. Kelly and P. J. Scheuer, *J. Nat. Prod.*, 2001, **64**, 1332.

298 K. D. Wellington, R. C. Cambie, P. R. Rutledge and P. R. Bergquist, *J. Nat. Prod.*, 2000, **63**, 79.

299 K. C. Nicolaou, D. Gray and J. Tae, *Angew. Chem. Int. Ed. Eng.*, 2001, **40**, 3679.

300 D. Tasdemir, G. P. Concepcion, G. C. Mangalindan, M. K. Harper, E. Hajdu and C. M. Ireland, *Tetrahedron*, 2001, **57**, 5681.

301 L. M. Zeng, Z. Guan, J. Y. Su, X. L. Feng, J. W. Cai, *Acta Chimica Sinica*, 2001, **59**, 1675.

302 M. McNally and R. J. Capon, *J. Nat. Prod.*, 2001, **64**, 645.

303 S. Yan, G. Zhang, J. Su and L. Zeng, *Gaodeng Xuexiao Huaxue Xuebao*, 2001, **22**, 949.

304 J. Tanaka, G. Marriott, T. Higa and T. Higa, *J. Nat. Prod.*, 2001, **64**, 1468.

305 A. D. Rodriguez and B. Vera, *J. Org. Chem.*, 2001, **66**, 6364.

306 R. J. Capon, E. L. Ghisalberti and P. R. Jefferies, *Experientia*, 1982, **38**, 1444.

307 R. J. Capon, A. Jenkins, F. Rooney and E. L. Ghisalberti, *J. Nat. Prod.*, 2001, **64**, 638.

308 J. Shin, J. R. Rho, Y. Seo, H. S. Lee, K. W. Cho and C. J. Sim, *Tetrahedron Lett.*, 2001, **42**, 3005.

309 Y. Liu, B. H. Bae, N. Alam, J. Hong, C. J. Sim, C. Lee, K. S. Im and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 1301.

310 K. A. El Sayed, M. T. Hamann, N. E. Hashish, W. T. Shier, M. Kelly and A. A. Khan, *J. Nat. Prod.*, 2001, **64**, 522.

311 R. P. Walker, J. E. Thompson and D. J. Faulkner, *J. Org. Chem.*, 1980, **45**, 4976.

312 Y. Noda, H. Hashimoto and T. Norizuki, *Heterocycles*, **55**, 1839.

313 R. D. Charan, T. C. McKee and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 661.

314 S. Kokubo, K. Yogi, M. J. Uddin, T. Inuzuka, K. Suenaga, K. Ueda and D. Uemura, *Chem. Lett*., 2001, 176.

315 M. S. Buchanan, A. Edser, G. King, J. Whitmore and R. J. Quinn, *J. Nat. Prod*., 2001, **64**, 300.

316 L. C. Chang, S. Otero-Quintero, G. M. Nicholas and C. A. Bewley, *Tetrahedron*, 2001, **57**, 5731.

317 W. A. Gallimore, M. Kelly and P. J. Scheuer, *J. Nat. Prod*., 2001, **64**, 741.

318 S. H. Xu and L. M. Zeng, *Youji Huaxue*, 2001, **21**, 45.

319 T. Miyamoto, K. Kodama, Y. Aramaki, R. Higuchi and R. W. M. van Soest, *Tetrahedron Lett*., 2001, **42**, 6349.

320 W. H. Lin, J. M. Fang and Y. S. Cheng, *Phytochemistry*, 1998, **48**, 1391.

321 W. Zhang and C. Che, *J. Nat. Prod*., 2001, **64**, 1489.

322 H. S. Lee, Y. Seo, J. R. Rho, J. Shin and V. J. Paul, *J. Nat. Prod*., 2001, **64**, 1474.

323 A. Rudi, T. Yosief, S. Loya, A. Hizi, M. Schleyer and Y. Kashman, *J. Nat. Prod*., 2001, **64**, 1451.

324 M. Fujita, Y. Nakao, S. Matsunaga, M. Seiki, Y. Itoh, R. W. M. van Soest, M. Heubes, D. J. Faulkner and N. Fusetani, *Tetrahedron*, 2001, **57**, 3885.

325 A. Qureshi and D. J. Faulkner, *Tetrahedron*, 1999, **55**, 8323.

326 M. L. Lerch and D. J. Faulkner, *Tetrahedron*, 2001, **7**, 4091.

327 S. Aoki, Y. Yoshioka, Y. Miyamoto, K. Higuchi, A. Setiawan, N. Murakami, Z. S. Chen, T. Sumizawa, S. Akiyama and M. Kobayashi, *Tetrahedron Lett*., 1998, **39**, 6303.

328 N. Murakami, M. Sugimoto, M. Morita and M. Kobayashi, *Chem. Eur. J*., 2001, **7**, 2663.

329 N. Shoji, A. Umeyama, K. Shin, K. Takeda, S. Arihara, J. Kobayashi and M. Takei, *J. Org. Chem.*, 1992, **57**, 2996.

330 M. E. Jung and T. W. Johnson, *Tetrahedron*, 2001, **57**, 1449.

331 K. M. Meragelman, T. C. McKee and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 389.

332 J. N. Tabudravu and M. Jaspars, *J. Nat. Prod.*, 2001, **64**, 813.

333 Y. Kashman, T. Yosief and S. Carmeli, *J. Nat. Prod.*, 2001, **64**, 175.

334 J. Kubanek, W. Fenical and J. R. Pawlik, *Nat. Prod. Lett.*, 2001, **15**, 275.

335 J. Shin, H. S. Lee, L. Woo, J. R. Rho, Y. Seo, K. W. Cho and C. J. Sim, *J. Nat. Prod.*, 2001, **64**, 767.

336 C. Campagnuolo, E. Fattorusso and O. Taglialatela-Scafati, *Tetrahedron*, 2001, **57**, 4049.

337 V. Costantino, E. Fattorusso, C. Imperatore and A. Mangoni, *Tetrahedron*, 2001, **57**, 4045.

338 S. Ohta, M. Uno, M. Tokumasu, Y. Hiraga and S. Ikegami, *Tetrahedron Lett.*, 1996, **37**, 7765.

339 H. Hioki, H. Ooi, M. Hamano, Y. Mimura, S. Yoshio, M. Kodama, S. Ohta, M. Yanai and S. Ikegami, *Tetrahedron*, 2001, **57**, 1235.

340 M. Ichihashi, H. Takikawa and K. Mori, *Biosci. Biotechnol. Biochem.*2001, **65**, 2569.

341 V. Costantino, E. Fattorusso, C. Imperatore and A. Mangoni, *Eur. J. Org. Chem.*, 2001, 4457.

342 J. Shin and W. Fenical, *Tetrahedron*, 1993, **49**, 9277.

343 T. W. Lee and E. J. Corey, *J. Am. Chem. Soc.*, 2001, **123**, 1872.

344 P. J. Sung, J. H. Su, C. Y. Duh, M. Y. Chiang and J. H. Sheu, *J. Nat. Prod.*, 2001, **64**, 318.

345 S. L. Wu, P. J. Sung, M. Y. Chiang, J. Y. Wu and J. H. Sheu, *J. Nat. Prod.*, 2001, **64**, 1415.

346 S. Aoki, M. Okano, K. Matsui, T. Itoh, R. Satari, S. Akiyama and M. Kobayashi, *Tetrahedron*, 2001, **57**, 8951.

347 J. H. Kwak, F. J. Schmitz and G. C. Williams, *J. Nat. Prod.*, 2001, **64**, 754.

348 A. Groweiss, S. A. Look and W. Fenical, *J. Org. Chem.*, 1988, **53**, 2401.

349 J. R. Rho, M. S. Oh, K. H. Jang, K. W. Cho and J. Shin, *J. Nat. Prod.*, 2001, **64**, 540.

350 A. Rueda, E. Zubia, M. J. Ortega and J. Salva, *J. Nat. Prod.*, 2001, **64**, 401.

351 N. Fusetani, H. Nagata, H. Hirota and T. Tsuyuki, *Tetrahedron Lett.*, 1989, **30**, 7079.

352 D. F. Taber and S. C. Malcolm, *J. Org. Chem.*, 2001, **66**, 944.

353 N. Gonzalez, M. A. Barral, J. Rodriguez and C. Jimenez, *Tetrahedron*, 2001, **57**, 3487.

354 Y. C. Shen, C. V. S. Prakash and Y. T. Chang, *Steroids*, 2001, **66**, 721.

355 Y. Seo, J. R. Rho, K. W. Cho and J. Shin, *Nat. Prod. Lett.*, 2001, **15**, 81.

356 A. D. Rodriguez and C. Ramirez, *J. Nat. Prod.*, 2001, **64**, 100.

357 A. D. Rodriguez and C. Ramirez, *Org. Lett.*, 2000, **2**, 507.

358 K. C. Nicolaou, G. Vassilikogiannakis, W. Mägerlein and R. Kranich, *Angew. Chem. Int. Ed. Eng.*, 2001, **40**, 2482.

359 M. Vanisree, G. V. Subbaraju and C. B. Rao, *J. Asian Nat. Prod. Res.*, 2001, **3**, 23.

360 A. D. Rodriguez, C. Ramirez, I. I. Rodriguez and E. Gonzalez, *Org. Lett.*, 1999, **1**, 527.

361 T. W. Johnson and E. J. Corey, *J. Am. Chem. Soc.*, 2001, **123**, 4475.

362 Y. P. Shi, A. D. Rodriguez and O. L. Padilla, *J. Nat. Prod.*, 2001, **64**, 1439.

363 F. J. Schmitz, D. J. Vanderah and L. S. Ciereszko, *J. Chem. Soc., Chem. Commun.*, 1974, 407.

364 O. M. Cobar, A. D. Rodriguez, O. L. Padilla and J. A. Sanchez, *J. Org. Chem.*, 1997, **62**, 7183.

365 A. Rueda, E. Zubia, M. J. Ortega and J. Salva, *Steroids*, 2001, **66**, 897.

366 S. P. Chen, P. J. Sung, C. Y. Duh, C. F. Dai and J. H. Sheu, *J. Nat. Prod.*, 2001, **64**, 1241.

367 A. Patra, A. Majumdar, K. K. Mandal, A. Ghosh, D. Banerjee and B. P. Haldar, *J. Indian Chem. Soc.*, 2001, **78**, 619.

368 M. Wessels, G. M. König and A. D. Wright, *J. Nat. Prod.*, 2001, **64**, 370.

369 M. F. Rodriguez Brasco, A. M. Seldes and J. A. Palermo, *Org. Lett.*, 2001, **3**, 1415.

370 L. M. Zeng, X. Q. Li, J. Y. Su, X. Fu and F. J. Schmitz, *J. Nat. Prod.*, 1995, **58**, 296.

371 J. G. Cui, L. M. Zeng, J. Y. Su and W. G. Lu, *Steroids*, 2001, **66**, 33.

372 G. H. Wang, J. H. Sheu, M. Y. Chiang and T. J. Lee, *Tetrahedron Lett.*, 2001, **42**, 2333.

373 W. Inman and P. Crews, *J. Org. Chem.*, 1989, **54**, 2526.

374 L. Xu, B. O. Patrick, M. Roberge, T. Allen, L. van Ofwegen and R. J. Andersen, *Tetrahedron*, 2000, **56**, 9031.

375 J. H. Sheu, G. H. Wang, P. J. Sung, C. Y. Duh and M. Y. Chiang, *Tetrahedron*, 2001, **57**, 7639.

376 P. Sharma and M. Alam, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2537.

377 D. Friedrich, R. W. Doskotch and L. A. Paquette, *Org. Lett.*, 2000, **2**, 1879.

378 Y. Uchio, M. Nakatani, T. Hase, M. Kodama, S. Usui and Y. Fukazawa, *Tetrahedron Lett.*, 1989, **30**, 3331.

379 Y. Uchio, M. Kodama, S. Usui and Y. Fukazawa, *Tetrahedron Lett.*, 1992, **33**, 1317.

380 F. Gallou, D. W. C. MacMillan, L. E. Overman, L. A. Paquette, L. D. Pennington and J. Yang, *Org. Lett.*, 2001, **3**, 135.

381 D. W. C. MacMillan, L. E. Overman and L. D. Pennington, *J. Am. Chem. Soc*., 2001, **123**, 9033.

382 P. Bernardelli, O. M. Moradei, D. Friedrich, J. Yang, F. Gallou, B. P. Dyck, R. W. Doskotch, T. Lange and L. A. Paquette, *J. Am. Chem. Soc*., 2001, **123**, 9021.

383 R. Britton, M. Roberge, H. Berisch and R. J. Andersen, *Tetrahedron Lett*., 2001, **42**, 2953.

384 T. Lindel, P. R. Jensen, W. Fenical, B. H. Long, A. M. Casazza, J. Carboni and C. R. Fairchild, *J. Am. Chem. Soc*., 1997, **119**, 8744.

385 B. Tursch, J. C. Braekman and D. Daloze, *Bull. Soc. Chim. Belg*., 1975, **84**, 767.

386 W. H. Zhang, I. D. Williams and C. T. Che, *Tetrahedron Lett*., 2001, **42**, 4681.

387 C. Y. Duh, M. C. Chia, S. K. Wang, H. J. Chen, A. A. H. El-Gamal and C. F. Dai, *J. Nat. Prod*., 2001, **64**, 1028.

388 M. Iwashima, K. Nara, Y. Nakamichi and K. Iguchi, *Steroids*, 2001, **66**, 25.

389 M. Kobayashi, N. K. Lee, B. W. Son, K. Yanagi, Y. Kyogoku and I. Kitagawa, *Tetrahedron Lett*., 1984, **25**, 5925.

390 K. Watanabe, M. Sekine, H. Takahashi and K. Iguchi, *J. Nat. Prod*., 2001, **64**, 1421.

391 C. Y. Duh, K. J. Chen, A. A. H. El-Gamal and C. F. Dai, *J. Nat. Prod*., 2001, **64**, 1430.

392 V. Anjaneyulu, P. V. Subba Rao, P. Radhika, H. Laatsch and R. N. Asolkar, *Indian J. Chem. Sect. B*., 2001, **40**, 405.

393 A. S. Dmitrenok, V. Anjaneyulu, P. V. Subba Rao, P. Radhika, P. S. Dmitrenok, V. M. Boguslavsky and V. A. Stonik, *Russ. Chem. Bull*., 2001, **50**, 1474.

394 P. Ramesh, V. Ravikanth and Y. Venkateswarlu, *Indian J. Chem. Sect. B*., 2001, **40**, 867.

395 T. V. Rezanka and V. M. Dembitsky, *Tetrahedron*, 2001, **57**, 8743.

396 A. M. Suleimenova, A. I. Kalinovskii, V. A. Raldugin, S. A. Shevtsov, I. Y. Bagryanskaya, Y. V. Gatilov, T. A. Kuznetsova and G. B. Elyalkov, *Khim. Prir. Soedin.*, 1988, **4**, 535.

397 T. Zhang, Z. Liu and Y. Li, *Synthesis*, 2001, **3**, 393.

398 Z. Yan, C. Chen and L. Zeng, *Redai Haiyang*, 1985, **4**, 80.

399 J. Su, S. Yan and L. Zeng, *Gaodeng Xuexiao Huaxue Xuebao*, 2001, **22**, 1515.

400 M. Kobayashi, T. Nakagawa and H. Mitsuhashi, *Chem. Pharm. Bull.*, 1979, **27**, 2382.

401 K. Mada, T. Ooi and T. Kusumi, *Spectroscopy*, 2001, **15**, 177.

402 J. Y. Su, R. L. Yang and L. M. Zeng, *Chin. J. Chem.*, 2001, **19**, 515.

403 K. Mori, K. Iguchi, N. Yamada, Y. Yamada and Y. Inouye, *Tetrahedron Lett.*, 1987, **28**, 5673.

404 H. Miyaoka, T. Baba, H. Mitome and Y. Yamada, *Tetrahedron Lett.*, 2001, **42**, 9233.

405 N. Alam, J. Hong, C. O. Lee, K. S. Im, B. W. Son, J. S. Choi, W. C. Choi and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 956.

406 N. Alam, B. H. Bae, J. Hong, C. O. Lee, K. S. Im and J. H. Jung, *J. Nat. Prod.*, 2001, **64**, 1059.

407 A. Athanasiadis, G. Anderluh, P. Macek and D. Turk, *Structure*, 2001, **9**, 341.

408 R. Zhuo, H. Fu, C. Zhong, X. Wang, W. Lin and L. Zhang, *Shengwu Huaxue Yu Shengwu Wuli Jinzhan*, 2001, **28**, 514.

409 J. S. Carlé and C. Christophersen, *J. Am. Chem. Soc.*, 1979, **101**, 4012.

410 P. Wulff, J. S. Carlé and C. Christophersen, *Comp. Biochem. Physiol.*, 1982, **71B**, 523.

411 P. Keil, E. G. Nielsen, U. Anthoni and C. Christophersen, *Acta Chem. Scand. B*, 1986, **40**, 555.

412 M. S. Morales-Ríos, O. R. Suárez-Castillo, J. J. Trujillo-Serrato and P. Joseph-Nathan, *J. Org. Chem.*, 2001, **66**, 1186.

413 P. B. Holst, U. Anthoni, C. Christophersen and P. H. Nielsen, *J. Nat. Prod.*, 1994, **57**, 997.

414 A. S. Cardoso, N. Srinivasan, A. M. Lobo and S. Prabhakar, *Tetrahedron Lett.*, 2001, **42**, 6663.

415 M. L. Ciavatta, E. Trivellone, G. Villani and G. Cimino, *Tetrahedron Lett.*, 1993, **34**, 6791.

416 M. V. Perkins and R. A. Sampson, *Org. Lett.*, 2001, 3, 123.

417 A. Spinella, E. Mollo, E. Trivellone and G. Cimino, *Tetrahedron*, 1997, **53**, 16891.

418 H. Takikawa, M. Yoshida and K. Mori, *Tetrahedron Lett.*, 2001, **42**, 1527.

419 M. Yoshida, H. Takikawa and K. Mori, *J. Chem. Soc. Perkin Trans. 1*, 2001, 1007.

420 H. Hioki, M. Hamano, M. Kubo, T. Uno and M. Kodama, *Chem. Lett.*, 2001, 898.

421 S. N. Fedorov, O. S. Radchenko, L. K. Shubina, A. I. Kalinovsky, A. V. Gerasimenko, D. Y. Popov and V. A. Stonik, *J. Am. Chem. Soc.*, 2001, **123**, 504.

422 C. R. Kaiser, L. F. Pitombo and A. C. Pinto, *Magn. Reson. Chem.*, 2001, **39**, 147.

423 D. R. Appleton, R. C. Babcock and B. R. Copp, *Tetrahedron*, 2001, **57**, 10181.

424 S. Araki, S. Yamada, S. Abe, H. Waki, K. Kon, S. Itonori, M. Sugita and S. Ando, *J. Biochem.*, 2001, **129**, 93.

425 A. Spinella, E. Zubia, E. Martinez, J. Ortea and G. Cimino, *J. Org. Chem.*, 1997, **62**, 5471.

426 T. V. Hansen and Y. Stenstrom, *Tetrahedron: Asymmetry*, 2001, **12**, 1407.

427 H. Kigoshi, T. Itoh, T. Ogawa, K. Ochi, M. Okada, K. Suenaga and K. Yamada, *Tetrahedron Lett.*, 2001, **42**, 7461.

428 Y. Sakio, Y. J. Hirano, M. Hayashi, K. Komiyama and M. Ishibashi, *J. Nat. Prod.*, 2001, **64**, 726.

429 E. D. de Silva, S. A. Morris, S. C. Miao, E. Dumdei and R. J. Andersen, *J. Nat. Prod.*, 1991, **54**, 993.

430 A. D. Lebsack, L. E. Overman and R. J. Valentekovich, *J. Am. Chem. Soc.*, 2001, **123**, 4851.

431 K. L. McPhail, M. T. Davies-Coleman and J. Starmer, *J. Nat. Prod.*, 2001, **64**, 1183.

432 N. Takada, K. Suenaga, K. Yamada, S. Z. Zheng, H. S. Chen and D. Uemura, *Chem. Lett.*, 1999, 1025.

433 K. Suenaga, K. Araki, T. Sengoku and D. Uemura, *Org. Lett.*, 2001, **3**, 527.

434 P. Ciminiello, E. Fattorusso, M. Forino, M. Di Rosa, A. Ianaro and R. Poletti, *J. Org. Chem.*, 2001, **66**, 578.

435 P. Ciminiello, C. Dell'Aversano, E. Fattorusso, M. Forino, S. Magno, A. Ianaro and M. Di Rosa, *Eur. J. Org. Chem.*, 2001, **1**, 49.

436 P. Ciminiello, C. Dell'Aversano, C. Fattorusso, E. Fattorusso, M. Forino and S. Magno, *Tetrahedron*, 2001, **57**, 8189.

437 N. Takada, N. Umemura, K. Suenaga, T. Chou, A. Nagatsu, T. Haino, K. Yamada and D. Uemura, *Tetrahedron Lett.*, 2001, **42**, 3491.

438 J. A. McCauley, K. Nagasawa, P. A. Lander, S. G. Mischke, M. A. Semones and Y. Kishi, *J. Am. Chem. Soc.*, 1998, **120**, 7647.

439 N. Takada, N. Umemura, K. Suenaga and D. Uemura, *Tetrahedron Lett.*, 2001, **42**, 3495.

440 N. Takada, M. Iwatsuki, K. Suenaga and D. Uemura, *Tetrahedron Lett.*, 2000, **41**, 6425.

441 H. Kigoshi, N. Hayashi and D. Uemura, *Tetrahedron Lett.*, 2001, **42**, 7469.

442 T. Chuo, M. Kuramoto, Y. Otani, M. Shikano, K. Yazawa and D. Uemura, *Tetrahedron Lett.*, 1996, **37**, 3871.

443 M. W. Carson, G. Kim and S. J. Danishefsky, *Angew. Chem. Int. Ed. Eng.*, 2001, **40**, 4453.

444 K. Ofuji, M. Satake, T. McMahon, K. J. James, H. Naoki, Y. Oshima and T. Yasumoto, *Biosci. Biotechnol. Biochem.*, 2001, **65**, 740.

445 T. Maoka, K. Hashimoto, N. Akimoto and Y. Fujiwara, *J. Nat. Prod.*, 2001, **64**, 578.

446 M. Tsushima, T. Maoka and T. Matsuno, *J. Nat. Prod.*, 2001, **64**, 1139.

447 N. M. Carballeira, H. Cruz, C. A. Hill, J. J. de Voss and M. Garson, *J. Nat. Prod.*, 2001, **64**, 1426.

448 A. Aiello, S. Carbonelli, E. Fattorusso, T. Iuvone and M. Menna, *J. Nat. Prod.*, 2001, **64**, 219.

449 A. Aiello, S. Carbonelli, G. Esposito, E. Fattorusso, T. Iuvone and M. Menna, *Org. Lett.*, 2001, **3**, 2941.

450 R. Britton, J. H. H. L. de Oliveira, R. J. Andersen and R. G. S. Berlinck, *J. Nat. Prod.*, 2001, **64**, 254.

451 L. H. Franco, E. B. de Kier Joffe, L. Puricelli, M. Tatian, A. M. Seldes and J. A. Palermo, *J. Nat. Prod.*, 1998, **61**, 1130.

452 P. M. Fresneda, P. Molina and J. A. Bleda, *Tetrahedron*, 2001, **57**, 2355.

453 A. Rudi and Y. Kashman, *J. Org. Chem.*, 1989, **54**, 5331.

454 I. Viracaoundin, R. Faure, E. M. Gaydou and M. Aknin, *Tetrahedron Lett.*, 2001, **42**, 2669.

455 B. R. Copp, J. W. Blunt, M. H. G. Munro and L. K. Pannell, *Tetrahedron Lett.*, 1989, **30**, 3703.

456 A. N. Pearce, R. C. Babcock, C. N. Battershill, G. Lambert and B. R. Copp, *J. Org. Chem.*, 2001, **66**, 8257.

457 M. J. Uddin, S. Kokubo, K. Suenaga, K. Ueda and D. Uemura, *Heterocycles*, 2001, **54**, 1039.

458 M. J. Uddin, S. Kokubo, K. Ueda, K. Suenaga and D. Uemura, *J. Nat. Prod.*, 2001, **64**, 1169.

459 H. Vervoort, W. Fenical and R. de A. Epifanio, *J. Org. Chem.*, 2000, **65**, 782.

460 B. Liang, D. J. Richard, P. S. Portonovo and M. M. Joullie, *J. Am. Chem. Soc.*, 2001, **123**, 4469.

461 A. Fontana, M. C. Gonzalez, M. Gavagnin, J. Templado and G. Cimino, *Tetrahedron Lett.*, 2000, **41**, 429.

462 R. Duran, E. Zubia, M. J. Ortega, S. Naranjo and J. Salva, *Tetrahedron*, 2000, **56**, 6031.

463 A. Fontana, G. Cimino, M. Gavagnin, M. C. Gonzalez and E. Estornell, *J. Med. Chem.*, 2001, **44**, 2362.

464 M. A. Exposito, B. Lopez, R. Fernandez, M. Vazquez, C. Debitus, T. Iglesias, C. Jimenez, E. Quinoa and R. Riguera, *Tetrahedron*, 1998, **54**, 7539.

465 A. Exposito, M. Fernandez-Suarez, T. Iglesias, L. Munoz and R. Riguera, *J. Org. Chem.*, 2001, **66**, 4206.

466 L. Garrido, E. Zubia, M. J. Ortega, S. Naranjo and J. Salva, *Tetrahedron*, 2001, **57**, 4579.

467 T. Ozawa, S. Aoyagi and C. Kibayashi, *J. Org. Chem.*, 2001, **66**, 3338.

468 B. Steffan, *Tetrahedron*, 1991, **47**, 8729.

469 J. Kubanek, D. E. Williams, E. D. de Silva, T. Allen and R. J. Andersen, *Tetrahedron Lett.*, 1995, **36**, 6189.

470 M. A. Rashid, K. R. Gustafson, L. K. Cartner, L. K. Pannell and M. R. Boyd, *Tetrahedron*, 2001, **57**, 5751.

471 M. C. McCoy and D. J. Faulkner, *J. Nat. Prod.*, 2001, **64**, 1087.

472 R. M. van Wagoner, J. Jompa, A. Tahir and C. M. Ireland, *J. Nat. Prod.*, 2001, **64**, 1100.

473 A. N. Pearce, R. C. Babcock, G. Lambert and B. R. Copp, *Nat. Prod. Lett.*, 2001, **15**, 237.

474 M. A. Rashid, K. R. Gustafson and M. R. Boyd, *J. Nat. Prod.*, 2001, **64**, 1454.

475 M. Wessels, G. M. König and A. D. Wright, *J. Nat. Prod.*, 2001, **64**, 1556.

476 T. N. Makarieva, A. S. Dmitrenok, P. S. Dmitrenok, B. B. Grebnev and V. A. Stonik, *J. Nat. Prod.*, 2001, **64**, 1559.

477 B. R. Copp, J. Jompa, A. Tahir and C. M. Ireland, *J. Org. Chem.*, 1998, **63**, 8024.

478 D. Skyler and C. H. Heathcock, *Org. Lett.*, 2001, **3**, 4323.

479 L. A. McDonald, G. S. Eldredge, L. R. Barrows and C. M. Ireland, *J. Med. Chem.*, 1994, **37**, 3819.

480 N. Lindquist, W. Fenical, G. D. van Duyne and J. Clardy, *J. Am. Chem. Soc.*, 1991, **113**, 2303.

481 J. Li, S. Jeong, L. Esser and P. G. Harran, *Angew. Chem. Int. Ed. Eng.*, 2001, **40**, 4765.

482 J. Li, A. W. G. Burgett, L. Esser, C. Amezcua and P. G. Harran, *Angew. Chem. Int. Ed. Eng.*, 2001, **40**, 4770.

483 C. Wang, G. Han, J. Su and L. Zeng, *Fenxi Huaxue*, 2001, **29**, 168.

484 I. H. Lee, Y. S. Lee, C. H. Kim, C. R. Kim, T. Hong, L. Menzel, L. M. Boo, J. Pohl, M. A. Sherman, A. Waring and R. I. Lehrer, *Biochim. Biophys. Acta*, 2001, **3**, 141.

485 R. I. Lehrer, I. H. Lee, L. Menzel, A. Waring and C. Zhao, *Adv. Exp. Med. Biol.*, 2001, **484**, 71.

486 K. Yamada, R. Matsubara, M. Kaneko, T. Miyamoto and R. Higuchi, *Chem. Pharm. Bull.*, 2001, **49**, 447.

487 N. V. Ivanchina, A. A. Kicha, A. I. Kalinovsky, P. S. Dmitrenok, N. G. Prokof'eva and V. A. Stonik, *J. Nat. Prod.*, 2001, **64**, 945.

488 N. Yayli, *Indian J. Chem. Sect. B.*, 2001, **40**, 399.

489 E. V. Levina, P. V. Andriyashchenko, A. I. Kalinovskii and V. A. Stonik, *Russ. Chem. Bull.*, 2001, **50**, 313.

490 K. Arao, M. Inagaki and R. Higuchi, *Chem. Pharm. Bull.*, 2001, **49**, 695.

491 A. A. Kicha, N. V. Ivanchina, A. I. Kalinovsky, P. S. Dmitrenok and V. A. Stonik, *Russ. Chem. Bull.*, 2001, **50**, 724.

492 M. S. Maier, A. J. Roccatagliata, A. Kuriss, H. Chludil, A. M. Seldes, C. A. Pujol and E. B. Damonte, *J. Nat. Prod.*, 2001, **64**, 732.

493 D. Sato, Y. Ando, R. Tsujimoto and K. Kawasaki, *Lipids*, 2001, **36**, 1371.

494 N. Takada, M. Watanabe, K. Suenaga, K. Yamada, M. Kita and D. Uemura, *Tetrahedron Lett.*, 2001, **42**, 6557.

495 A. P. Murray, C. Muniain, A. M. Seldes and M. S. Maier, *Tetrahedron*, 2001, **57**, 9563.

496 S. Urban, S. J. H. Hickford, J. W. Blunt, M. H. G. Munro and M. Kelly, *Current Organic Chemistry*, 2000, **7**, 765.

497 D. J. Faulkner, *Nat. Prod. Rep.*, 2002, **19**, 1.